SEARCH REQUEST FORM

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Scientific and Technical Information Center

Requester's Full Name: SHANON FOLEY Examiner #: 77851 Date: 4/17/01
Art Unit: 1648 Phone Number 308-3983 Serial Number: 09/606,011
Mail Box and Bldg/Room Location: 8E12/8009 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Immunogenic complexes and methods relating thereto

Inventors (please provide full names): John Cooper COX; Debbie Pauline DRANE
Andreas SUHRBIER

Earliest Priority Filing Date: 2/17/99

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please include an inventor name search.

Please search for an immunogenic complex or vaccine that comprises ① a complex with a naturally charged adjuvant (lipid A and/or saponin (ISCOMATRIX)) that has been modified to increase negative charge and ② a positively charged antigen that has been modified to increase positive charge.

This complex induces cyto toxic T cell responses + improves microbial infection;

Cancer; HIV; Hepatitis B, C; tuberculosis,
↳ (melanoma) prostate cancer, breast cancer.

Thank you

Point of Contact:
Beverly Shears
Technical Info. Specialist
CM1 12C14 Tel: 308-4994

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TECH CENTER 1600/2900

Please give to Beverly Shears.

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: Beverly @ 4994	NA Sequence (#)	STN ✓
Searcher Phone #:	AA Sequence (#)	Dialog
Searcher Location:	Structure (#)	Questel/Orbit
Date Searcher Picked Up:	Bibliographic	Dr.Link
Date Completed: 04-24-01	Litigation	Lexis/Nexis
Searcher Prep & Review Time: 12	Fulltext	Sequence Systems
Clerical Prep Time:	Patent Family	WWW/Internet
Online Time: 50	Other	Other (specify)

PTO-1590 (1-2000)

Foley, S.
09/506011


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     (FILE 'REGISTRY' ENTERED AT 11:35:38 ON 24 APR 2001)
                  E SAPPONIN/CN 5
                  E SAPONIN/CN 5
L5              1 S E3
                  E ISCOMATRIX/CN 5
                  E PHOSPHOLIPID/CN 5
                  E PHOSPHOLIPIDS/CN 5
L6              1 S E3
                  E PHOSPHOGLYCERIDE/CN 5
L7              1 S E5
                  E PHOSPHATIDYL INOSITOL/CN 5
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                  E PHOSPHATIDYL GLYCEROL/CN 5
                  E INOSITOL, PHOSPHATIDYL/CN 5
                  E INOSITOL, GLYCEROL/CN 5
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                  E INOSITOLS, PHOSPHATIDYL/CN 5
                  E CARDIOLIPIN/CN 5
                  E LIPID A/CN 5
                  E DIPHOSPHORYL LIPID A/CN 5
                  E MONOPHOSPHORYL LIPID A/CN 5
L8              2 S E3
                  E OM 174/CN 5
L9              1 S E3
L10             6 S L5 OR L6 OR L7 OR L8 OR L9

                  E PHOSPHATIDIC ACID/CN 5
L18             1 S E22
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Searcher : Shears 308-4994

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=> fil reg; d que l8; fil caplu; d que l14; d que l15; s l14 or l15
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DICTIONARY FILE UPDATES:  23 APR 2001  HIGHEST RN 332094-77-6

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

  Please note that search-term pricing does apply when
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Structure search limits have been increased.  See HELP SLIMIT
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L1   (         1)SEA FILE=REGISTRY ABB=ON  PLU=ON  SAPONIN/CN
L2   (         1)SEA FILE=REGISTRY ABB=ON  PLU=ON  PHOSPHOLIPIDS/CN
L3   (         1)SEA FILE=REGISTRY ABB=ON  PLU=ON  PHOSPHOGLYCERIDES/CN
L4   (         2)SEA FILE=REGISTRY ABB=ON  PLU=ON  "MONOPHOSPHORYL LIPID
                 A"/CN
L5   (         1)SEA FILE=REGISTRY ABB=ON  PLU=ON  "OM 174"/CN
L6   (         6)SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2 OR L3 OR L4
                 OR L5
L7   (         1)SEA FILE=REGISTRY ABB=ON  PLU=ON  "PHOSPHATIDIC ACIDS"/CN

L8             7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 OR L7

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FILE LAST UPDATED: 23 Apr 2001  (20010423/ED)

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L1   (         1) SEA FILE=REGISTRY ABB=ON  PLU=ON  SAPONIN/CN
L2   (         1) SEA FILE=REGISTRY ABB=ON  PLU=ON  PHOSPHOLIPIDS/CN
L3   (         1) SEA FILE=REGISTRY ABB=ON  PLU=ON  PHOSPHOGLYCERIDES/CN
L4   (         2) SEA FILE=REGISTRY ABB=ON  PLU=ON  "MONOPHOSPHORYL LIPID
                  A"/CN
L5   (         1) SEA FILE=REGISTRY ABB=ON  PLU=ON  "OM 174"/CN
L6   (         6) SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2 OR L3 OR L4
                  OR L5
L7   (         1) SEA FILE=REGISTRY ABB=ON  PLU=ON  "PHOSPHATIDIC ACIDS"/CN

L8             7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 OR L7
L9        406206 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 OR CARRIER OR
                  ADJUVANT OR SAPONIN OR ISCOMATRIX OR PHOSPHOLIPID OR
                  PHOSPHOGLYCERIDE OR PHOSPHO(W)(LIPID OR GLYCERIDE) OR
                  PHOSPHATIDYL(W)(INOSITOL OR GLYCERIDE) OR PHOSPHATIDYLINO
                  SITOL OR PHOSPHATIDYLGLYCERIDE OR PHOSPHATIDIC OR
                  CARDIOLIPIN OR LIPID(W)A OR CARDIO LIPIN OR OM174 OR OM
                  174
L10        75472 SEA FILE=CAPLUS ABB=ON  PLU=ON  L9 AND (ANTIGEN OR
                  PROTEIN)
L11         2584 SEA FILE=CAPLUS ABB=ON  PLU=ON  L10 AND CHARG?
L12          619 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 AND POSITIV?
L13          337 SEA FILE=CAPLUS ABB=ON  PLU=ON  L12 AND NEGATIV?
L14            5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L13 AND ((CYTOTOX? OR
                  CYTO TOX?)(S)(T(W)(CELL OR LYMPHOCYT?)))
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-misspelling; Re-searched, see last pgs.

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L1   (         1) SEA FILE=REGISTRY ABB=ON  PLU=ON  SAPONIN/CN
L2   (         1) SEA FILE=REGISTRY ABB=ON  PLU=ON  PHOSPHOLIPIDS/CN
L3   (         1) SEA FILE=REGISTRY ABB=ON  PLU=ON  PHOSPHOGLYCERIDES/CN
L4   (         2) SEA FILE=REGISTRY ABB=ON  PLU=ON  "MONOPHOSPHORYL LIPID
                  A"/CN
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Searcher : Shears 308-4994

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L5  (         1)SEA FILE=REGISTRY ABB=ON  PLU=ON  "OM 174"/CN
L6  (         6)SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2 OR L3 OR L4
                OR L5
L7  (         1)SEA FILE=REGISTRY ABB=ON  PLU=ON  "PHOSPHATIDIC ACIDS"/CN

L8            7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 OR L7
L9       406206 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 OR CARRIER OR
                ADJUVANT OR SAPONIN OR ISCOMATRIX OR PHOSPHOLIPID OR
                PHOSPHOGLYCERIDE OR PHOSPHO(W)(LIPID OR GLYCERIDE) OR
                PHOSPHATIDYL(W)(INOSITOL OR GLYCERIDE) OR PHOSPHATIDYLINO
                SITOL OR PHOSPHATIDYLGLYCERIDE OR PHOSPHATIDIC OR
                CARDIOLIPIN OR LIPID(W)A OR CARDIO LIPIN OR OM174 OR OM
                174
L10       75472 SEA FILE=CAPLUS ABB=ON  PLU=ON  L9 AND (ANTIGEN OR
                PROTEIN)
L11        2584 SEA FILE=CAPLUS ABB=ON  PLU=ON  L10 AND CHARG?
L12         619 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 AND POSITIV?
L13         337 SEA FILE=CAPLUS ABB=ON  PLU=ON  L12 AND NEGATIV?
L15          16 SEA FILE=CAPLUS ABB=ON  PLU=ON  L13 AND (INFECTION OR
                HIV OR HTLV OR AIDS OR HUMAN(3W)VIRUS OR ACQUIRED(2W)SYND
                ROM? OR HEPATIT? OR TB OR TUBERCULOS? OR PARASIT?(3A)(CON
                DITION OR DISEAS? OR DISORDER) OR MELANOM?)

L16          20 L14 OR L15

L16  ANSWER 1 OF 20  CAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:        2000:786836  CAPLUS
TITLE:                   Evaluation of a liposome-supplemented intranasal
                         influenza subunit vaccine in a murine model
                         system: Induction of systemic and local mucosal
                         immunity
AUTHOR(S):               de Haan, Aalzen; van Scharrenburg, Guus J. M.;
                         Masihi, K. Noel; Wilschut, Jan
CORPORATE SOURCE:        Department of Medical Microbiology, Molecular
                         Virology Section, University of Groningen,
                         Groningen, 9713 AV, Neth.
SOURCE:                  J. Liposome Res. (2000), 10(2 & 3), 159-177
                         CODEN: JLREE7; ISSN: 0898-2104
PUBLISHER:               Marcel Dekker, Inc.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   This study reports on the mucosal immunoadjuvant activity of
     liposomes in an exptl. influenza subunit vaccine administered
     intranasally (i.n.) to mice. Antibody responses induced by the i.n.
     liposomal vaccine were compared to those induced by an influenza
     infection or by s.c. (s.c.) injection of subunit
     antigen alone, the conventional route of human flu
     vaccination. Neg. charged liposomes, but not
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pos. charged or zwitterionic liposomes, coadministered i.n. with influenza subunit **antigen**, significantly stimulated systemic IgG levels and local antibody responses in pulmonary secretions, relative to the responses upon i.n. administration of subunit **antigen** alone. I.n. immunization with liposome-supplemented subunit **antigen** as well as s.c. immunization with subunit **antigen** alone or **infection**. Induced high levels of IgG antibodies in serum and pulmonary secretions, with a preferential induction of IgG1 upon immunization and IgG2a upon **infection**. Both i.n. immunization with liposome-supplemented **antigen** and **infection**, but not s.c. immunization with subunit **antigen** alone, induced local secretion of S-IgA. At the same time, both IgA- and IgG-secreting cells appeared in the lungs and lung-assocd. lymph nodes, suggestive of local antibody prodn. In conclusion, the liposomal **adjuvant** system, combined with a mucosal administration protocol, provides a promising strategy for induction of both systemic and local antibody responses against influenza virus.

REFERENCE COUNT: 48

REFERENCE(S):
(1) Alving, C; Biochim Biophys Acta 1992, V1113, P307 CAPLUS
(3) Ben Ahmeida, E; Arch Virol 1992, V125, P71 CAPLUS
(11) De Haan, A; Immunology 1996, V89, P488 CAPLUS
(12) De Haan, A; Vaccine 1995, V13, P1320 CAPLUS
(13) De Haan, A; Vaccine 1995, V13, P155 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:592580 CAPLUS
DOCUMENT NUMBER: 133:191986
TITLE: Immunogenic complexes and methods relating thereto
INVENTOR(S): Cox, John Cooper; Drane, Debbie Pauline
PATENT ASSIGNEE(S): CSL Limited, Australia
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000048630	A1	20000824	WO 2000-AU110	20000217

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,

CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 1999-8735 A 19990217
AU 1999-1861 A 19990727

AB The present invention relates generally to an immunogenic complex comprising a **charged** org. **carrier** and a **charged antigen** and, more particularly, a **neg. charged** org. **carrier** and a **pos. charged antigen**. The complexes of the present invention are useful, inter alia , as therapeutic and/or prophylactic agents for facilitating the induction of a **cytotoxic T-lymphocyte** response to an **antigen**.

IT **171092-39-0, OM 174**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunogenic complexes **neg. charged** org. **carrier** and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

REFERENCE COUNT: 5
REFERENCE(S):
(1) Callahan, P; Pharmaceutical Research 1991, V8(7), P851 CAPLUS
(2) Friede, M; Molecular Immunology 1993, V30(6), P539 CAPLUS
(3) Morein; EP 0109942 A 1984 CAPLUS
(4) Morein; EP 0180564 A 1986 CAPLUS
(5) Nakanishi, T; Biochemical and Biophysical Research Communications 1997, V240(3), P793 CAPLUS

L16 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:526177 CAPLUS
DOCUMENT NUMBER: 134:250883
TITLE: Influence of antigenic forms and **adjuvants** on protection against a lethal **infection** of Aujeszky's disease virus
AUTHOR(S): Katayama, S.; Oda, K.; Ohgitani, T.
CORPORATE SOURCE: Division of Veterinary Microbiology, Kyoto Biken Laboratories, Uji, Kyoto, 611-0041, Japan
SOURCE: Vaccine (2000), 19(1), 54-58
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The influence of antigenic forms and **adjuvant** types on protection against a lethal **infection** of Aujeszky's disease virus (ADV) in mice was investigated. Antiviral IgG2a antibody response against particulate (inactivated ADV) and sol. **antigen** (ADV solubilized with deoxycholate-Na) in approx. order of extent was ISA70 > QS-21 > **pos. charged** liposome > **neg. charged** liposome > weak **neg. charged** liposome > ISA25 > lablabside F **saponin** > aluminum phosphate gel > non **adjuvant**. Particulate **antigen** induced higher IgG2a antibody prodn. than sol. **antigen**. Particulate **antigen** combined with ISA70, ISA25 or **pos. charged** liposome gave 100, 50 and 40% protection to mice, resp. In contrast, sol. **antigen** plus ISA70 conferred 30% protection on mice. Immunogens using the other **adjuvants** gave .ltoreq.20% protection to mice. These results indicate that a combination of particulate **antigen** and an appropriate **adjuvant** effectively induces the prodn. of antiviral IgG2a antibody and provides protection against a lethal ADV **infection** in mice.
REFERENCE COUNT: 35
REFERENCE(S): (1) Akiyama, Y; Cancer Res 1984, V44, P5127 CAPLUS
(2) Aramaki, Y; Vaccine 1995, V13, P1809 CAPLUS
(3) Baca-Estrada, M; Vaccine 1997, V15, P1753 CAPLUS
(4) Beck, L; Cell Immunol 1989, V123, P1 CAPLUS
(5) Boere, W; Immunology 1986, V58, P553 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:84830 CAPLUS
DOCUMENT NUMBER: 132:136417
TITLE: Synthetic peptides and methods of use for autoimmune disease therapies
INVENTOR(S): Strominger, Jack L.; Fridkis-Hareli, Masha
PATENT ASSIGNEE(S): The President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000005249	A2	20000203	WO 1999-US16617	19990722
WO 2000005249	A3	20001005		

W: AU, CA, IL, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AU 9952234	A1	20000214	AU 1999-52234	19990722

PRIORITY APPLN. INFO.:
US 1998-93859 P 19980723
US 1999-123675 P 19990309
WO 1999-US16617 W 19990722

AB The invention provides heteropolymer compns. and peptide compns., and methods of making and using therapeutic compns. comprising amino acid heteropolymers for treatment of a subject for an autoimmune or an inflammatory disease, the heteropolymer compns. made by solid state synthesis. The invention also provides kits for assaying binding of a compn. to a water-sol. MHC **protein**.

L16 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:18146 CAPLUS
DOCUMENT NUMBER: 132:175336
TITLE: **Charge** modification of plasma and milk **proteins** results in antiviral active compounds
AUTHOR(S): Swart, Pieter J.; Harmsen, Martin C.; Kuipers, Mirjam E.; Van'Dijk, Alard A.; Van Der Strate, Barry W. A.; Van Berkel, Patrick H. C.; Nuijens, Jan H.; Smit, Catharina; Witvrouw, Miryam; De Clercq, Erik; De Bethune, Marie-Pierre; Pauwels, Rudi; Meijer, K. F.
CORPORATE SOURCE: Department of Pharmacokinetics and Drug Delivery, University Centre for Pharmacy, Groningen University Institute for Drug Exploration (GUIDE), Groningen, 9713 AV, Neth.
SOURCE: J. Pept. Sci. (1999), 5(12), 563-576
CODEN: JPSIEI; ISSN: 1075-2617
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous studies have shown that acylated plasma and milk **proteins** with increased **neg. charge**, derived from various animal and human sources, are potent anti-**HIV** compds. The antiviral effects seemed to correlate **pos.** with the no. of **neg. charges** introduced into the various polypeptides: **proteins** with a high content of basic amino acids in which all of the available .epsilon.NH2 groups were anionized yielded the most potent anti-**HIV** compds. It remained unclear however whether the total net **neg. charge** of the various derivatized

prot ins, or rather the **charge** d. on the **protein** backbone, is essential for the obsd. anti-**HIV** activity. Earlier studies have shown that acylated albumins preferentially block the process of **HIV**/cell fusion through binding to the **HIV** envelope **proteins** gp120 and gp41 as well as to the cell surface of the **HIV** target cells. Some of these polyanionic **proteins** have been shown to interfere also with the gp120-CD4 mediated virus/cell binding. The relative contribution of these effects to the anti-**HIV** activity may depend both on the total **neg. charge** introduced as well as the hydrophobicity of the acylating reagent added to the particular **proteins**. In this study the authors show that the higher the **charge** d. of the derivatized **proteins**, the more potent their **HIV** replication inhibiting effects are. In contrast, the addn. of **pos. charge** to the studied plasma and milk **proteins** through amination resulted in a reduced anti-**HIV** activity but a clearly increased anti-HCMV activity, with IC50 values in the low micromolar concn. range. Interestingly, native lactoferrin (Lf) was antivirally active against both **HIV** and HCMV. Acylation or amination of Lf increased the anti-**HIV** and anti-HCMV activity, resp. The N-terminal portion of Lf appeared essential for its anti-HCMV effect: N-terminal deletion variants of human Lf were less active against HCMV. CD of the modified **proteins** showed that the secondary structure of the tested **proteins** was only moderately influenced by acylation and/or covalent attachment of drugs, making these (derivatized) **proteins** useful candidates as antiviral agents and/or intrinsically active drug **carriers**. The relatively simple chem. derivatization as well as the abundant sources of blood plasma and milk **proteins** provides attractive opportunities for the prepn. of potent and relatively cheap antiviral agents for systemic or local applications.

REFERENCE COUNT: 44
REFERENCE(S):
(2) Banga, A; Pharm Res 1993, V10, P697 CAPLUS
(3) Batra, P; J Protein Chem 1989, V8, P609 CAPLUS
(4) Berkhout, B; AIDS Res Hum Retroviruses 1997, V13, P1101 CAPLUS
(5) Cerenzia, M; Hepatology 1996, V23, P657 CAPLUS
(6) Collier, A; New Engl J Med 1996, V334, P1011 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:557808 CAPLUS

DOCUMENT NUMBER: 131:341812
TITLE: **Positively charged** liposome functions as an efficient immunoadjuvant in inducing cell-mediated immune response to soluble **proteins**
AUTHOR(S): Nakanishi, T.; Kunisawa, J.; Hayashi, A.; Tsutsumi, Y.; Kubo, K.; Nakagawa, S.; Nakanishi, M.; Tanaka, K.; Mayumi, T.
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Osaka University, Osaka, Japan
SOURCE: J. Controlled Release (1999), 61(1-2), 233-240
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to design an optimized liposome immunoadjuvant for inducing cell-mediated immune response against sol. proteinaceous **antigens**, we investigated the effect of liposomal surface **charge** on the immunoadjuvant action. **Pos. charged** liposomes contg. sol. **antigens** functioned as a more potent inducer of **antigen**-specific **cytotoxic T lymphocyte** responses and delayed type hypersensitivity response than **neg. charged** and neutral liposomes contg. the same concns. of **antigens**. To clarify the reason of the differential immune response, we examd. the delivery of sol. **proteins** by the liposomes into the cytoplasm of macrophages, using fragment A of diphtheria toxin (DTA) as a marker. We found that **pos. charged** liposomes encapsulating DTA are cytotoxic to macrophages, while empty **pos. charged** liposomes, DTA in **neg. charged** and neutral liposomes are not. Consistent with this, only macrophages pulsed with OVA in **pos. charged** liposomes could significantly stimulate OVA-specific, class I MHC-restricted T cell hybridoma. These results suggest that the **pos. charged** liposomes can deliver proteinaceous **antigens** efficiently into the cytoplasm of the macrophages/**antigen**-presenting cells, where the **antigens** are processed to be presented by class I MHC mols. to induce the cell-mediated immune response. Possible development of a safe and effective vaccine is discussed.
REFERENCE COUNT: 38
REFERENCE(S):
(1) Abraham, E; J Immunol 1992, V149(11), P3719 CAPLUS
(2) Alving, C; J Immunol Methods 1991, V140(1), P1 CAPLUS
(4) Aramaki, Y; Eur J Pharm Sci 1995, V3, P63 CAPLUS
(5) Bender, A; J Exp Med 1995, V182(6), P1663

CAPLUS
(8) Carbone, F; J Exp Med 1990, V171(2), P377
CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:191229 CAPLUS
DOCUMENT NUMBER: 131:30944
TITLE: Antiphosphatidylserine antibodies in patients with autoimmune diseases and **HIV** -infected patients: effects of Tween 20 and relationship with antibodies to .beta.2-glycoprotein I
AUTHOR(S): Gonzalez, Concepcion; Leston, Antonio; Garcia-Berrocal, Belen; Sanchez-Rodriguez, Angel; Martin-Oterino, Jose A.; Alberca, Ignacio; Cordero, Miguel; Jorge, Ramon; Navajo, Jose A.; Gonzalez-Buitrago, Jose M.
CORPORATE SOURCE: Servicio de Bioquimica, Hospital Universitario, Salamanca, 37007, Spain
SOURCE: J. Clin. Lab. Anal. (1999), 13(2), 59-64
CODEN: JCANEM; ISSN: 0887-8013
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Antiphospholipid antibodies (aPL) react with **neg. charged phospholipids**, which may often be complexed with a **protein** cofactor such as .beta.2 glycoprotein (.beta.2GPI) and prothrombin. Cofactor requirements may be assessed by measuring antibodies to .beta.2GPI or by adding Tween 20 to some reagents in the assays for aPL (anticardiolipin and antiphosphatidylserine). We have measured anticardiolipin antibodies (aCL), antiphosphatidylserine antibodies (aPS), and anti .beta.2 glycoprotein antibodies (a.beta.2GPI) in the serum of 10 normal subjects, 20 patients with systemic autoimmune diseases (SAD) diagnosed as having systemic lupus erythematosus (SLE) or antiphospholipid syndrome (APS), and 12 patients with **HIV infection**. Adding Tween 20 to aPS, the assay could not differentiate **protein** cofactor dependent from independent antibodies, but this can be done by measuring a.beta.2GPI. There was a significant correlation between aCL and a.beta.2GPI in the control group and in the patients with SAD, but not in the **HIV-pos**. (**HIV+**) patients. After excluding the **HIV+** patients, the best Spearman correlation was obtained between a.beta.2GPI and aCL. In 3 out of 7 patients with **pos**. a.beta.2GPI and in 5 out of 6 patients with moderate or high **pos**. aCL of the group of SAD, there was a history of venous thrombosis. The presence of moderate or high

values of aCL either alone or together with a.beta.2GPI was significantly assocd. with a history of venous thrombosis. Moderate or high aCL concns. and their assocn. with a.beta.2GPI seems to be useful for the assessment of the risk of venous thrombosis in unselected patients with SLE or APS.

REFERENCE COUNT: 22

REFERENCE(S):
(4) Cines, D; J Clin Immunol 1995, V15, P86S CAPLUS
(8) Forastiero, R; Thromb Haemost 1996, V75, P717 CAPLUS
(9) Harris, E; Br J Haematol 1990, V74, P1 CAPLUS
(12) McNeil, H; Adv Immunol 1991, V49, P193 CAPLUS
(13) McNeil, H; Proc Natl Acad Sci U S A 1990, V87, P4120 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:685735 CAPLUS

DOCUMENT NUMBER: 130:37043

TITLE: Patterns of circulating **hepatitis** B surface **antigen** variants among vaccinated children born to **hepatitis** B surface **antigen carrier** and non-**carrier** mothers. A population-based comparative study

AUTHOR(S): Ho, Mei-Shang; Mau, Yi-Chien; Lu, Chih-Feng; Huang, Shiang-Fen; Hsu, Li-Ching; Lin, Sheue-Rong; Hsu, Hsu-Mei

CORPORATE SOURCE: Div. Epidemiology Public Health, Inst. Biomedical Sciences, Academica Sinica, Taipei, 11529, Taiwan

SOURCE: J. Biomed. Sci. (Basel) (1998), 5(5), 355-362
CODEN: JBCIEA; ISSN: 1021-7770

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Hepatitis** B virus (HBV) variants that possessed missense mutation within the neutralization epitope of the major S **antigen** as defined by amino acid residues 124-147, termed the "a" determinant variants, were identified through a population-based sero-survey of 2305 children of the vaccinated birth cohorts born after 1986. Data on the 678 nucleotides encoding the S **antigen** of HBV were available for 75 HBV strains that were collected from 63 vaccinated children and 12 unvaccinated or incompletely vaccinated children, and 21 HBV strains from 25 unvaccinated adults. Among the diverse patterns of 1-three amino

acid substitutions within the "a" determinant, 145-Arg occurred most frequently (5/14); other variants were: 126-Ala, 127-Thr, 126-Ser/131-Asn/133-Thr, 129-His, 129-Arg, 123-Asn/131-Ile, 133-Leu, 141-Glu, and 141-Arg/144-Ala. Only one of these variants occurred in the 16 **hepatitis** B surface **antigen** (HBsAg)-**carrier** children born to HBsAg-**neg**. mothers, whereas 12 of these variants occurred in the 20 (50%) children born to HBsAg-**pos**. mothers. Early administration of HBV vaccine within the neonatal period increased the likelihood of the emergence of these variants to 64.7% (11/17). Five of the 21 (23.8%) unvaccinated HBsAg-**carrier** adults harbored the "a" determinant variants possessing mutations within 125-136, i.e. the putative 1st loop formed by the Cys disulfide bonds. Vaccinated children were likely to harbor HBV variants possessing mutations involving altered **charge** of side chains and/or its hydrophobicity of amino acid residues within the putative 2nd loop between 140 and 146. These data suggest that emergence of these HBV S gene mutants in the phase of HBV vaccination program would be most common among populations in whom perinatal/vertical transmission of HBV is most common, i.e. southeast Asian and the Taiwanese.

REFERENCE COUNT: 34

REFERENCE(S):
(1) Arauz-Ruiz, P; J Infect Dis 1997, V176, P851 CAPLUS
(4) Blum, H; Intervirology 1993, V35, P40 CAPLUS
(7) Carman, W; Lancet 1995, V345, P1406 CAPLUS
(8) Chiou, H; J Gen Virol 1997, V78, P2639 CAPLUS
(11) Hino, K; Dig Dis Sci 1995, V40, P566 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:497103 CAPLUS
DOCUMENT NUMBER: 129:274369
TITLE: Cationization of liposomal surface **charge** enhances **adjuvant** effect of liposomes for tumor vaccine
AUTHOR(S): Nakanishi, Tsuyoshi; Kunisawa, Jun; Hayashi, Akira; Tsutsumi, Yasuo; Hayakawa, Takao; Mayumi, Tadanori
CORPORATE SOURCE: Graduate School of Pharmaceutical Science, Osaka University, Suita, Osaka, 565-0871, Japan
SOURCE: Yakuzaigaku (1998), 58(2), 59-68
CODEN: YAKUA2; ISSN: 0372-7629
PUBLISHER: Nippon Yakuzai Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In order to design an optimum liposome immunoadjuvant for tumor vaccines, we investigated the relationship between liposome surface

charge and **adjuvant** action. **Pos**. **charged** multilamellar vesicles (MLVs) were taken up efficiently by macrophages, while **neg**. **charged** and neutral MLVs were hardly picked up. Consistent with this, **p s**. **charged** MLVs contg. sol. ovalbumin (OVA) functioned as a more potent inducer of **antigen**-specific **cytotoxic T lymphocyte** (CTL) responses and antibody prodn. than **neg**. **charged** and neutral MLVs contg. the same concns. of **antigens**. Furthermore, the in vivo anti-tumor effects of variously **charged** liposomal **antigens** were examd. using a Meth A tumor model and a crude butanol ext. derived from Meth A (Meth A-CBE) as the tumor-assocd. **antigen**. Mice vaccinated with **pos**. **charged** MLVs contg. Meth A-CBE showed significant inhibition of Meth A tumor growth compared to mice vaccinated with Meth A-CBE alone or mice vaccinated with neutral or **neg**. **charged** liposomal Meth A-CBE. The injection of carrageenan into mice led to a significant loss of anti-tumor vaccinal effect of **pos**. **charged** liposomal Meth A-CBE, which may be due to the inhibition of uptake and **antigen** presentation of liposomal **antigens** by macrophages as a result of a lack of macrophages in the immune site. Our results indicate that the **pos**. **charge** on the surface of liposomes represents an important factor for enhancing their immunoadjuvancy in the induction of **antigen** -specific immune responses and vaccinal effects against tumors.

L16 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:466906 CAPLUS
DOCUMENT NUMBER: 129:199563
TITLE: Interaction of a basic amphipathic peptide from the carboxyterminal part of the **HIV** envelope **protein** gp41 with **negatively charged** lipid surfaces
AUTHOR(S): Trommeshauser, Dirk; Galla, Hans-Joachim
CORPORATE SOURCE: Institute of Biochemistry, Westfalische Wilhelms-Universitat Munster, Munster, D-48149, Germany
SOURCE: Chem. Phys. Lipids (1998), 94(1), 81-96
CODEN: CPLIA4; ISSN: 0009-3084
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The interaction of the **pos**. **charged** synthetic amphipathic peptide fragment gp41828 corresponding to a segment from the carboxyterminal region of the **HIV** envelope glycoprotein gp41 with lipid monolayers spread at the air-water

interface has been studied by film balance measurements. The peptide itself does not form a stable monolayer but interacts with **phospholipids** spread together on the aq. surface. Upon compression of a mixed phosphatidylcholine-peptide monolayer the peptide is irreversibly squeezed out of the lipid-peptide monolayer. In contrast, with **neg. charged** phosphatidylglycerol stable lipid-peptide monolayers are formed even in the presence of up to 30 mol% peptide. The monolayer may be expanded and compressed repeatedly without significant loss of substance. After addn. of calcium ions to the subphase of a phosphatidylglycerol-peptide monolayer the peptide is to some extent excluded from the monolayer. In contrast to phosphatidylcholine monolayers this process is partly reversible and the excluded material is reincorporated into the film during subsequent expansion. We conclude that attached to the headgroups of the lipid monolayer a peptide-layer stabilized at the surface by electrostatic interactions is formed. The surface action may lead to rigidified lipid-peptide domains causing an increased membrane permeability which might correspond to a cytopathol. function of the **protein** fragment.

L16 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:89265 CAPLUS
DOCUMENT NUMBER: 128:153144
TITLE: Identification of short peptide sequences representing epitopes of glycoprotein G of HSV-2 using a phage peptide display library for use in an anti-gG2 ELISA
INVENTOR(S): Grabowska, Anna Marie; Irving, William Lucien; Laing, Peter
PATENT ASSIGNEE(S): Peptide Therapeutics Ltd., UK; Grabowska, Anna Marie; Irving, William Lucien; Laing, Peter
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9803544	A1	19980129	WO 1997-GB2003	19970724

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9736309	A1	19980210	AU 1997-36309	19970724
PRIORITY APPLN. INFO.:			GB 1996-15533	19960724
			WO 1997-GB2003	19970724

AB The invention provides a polypeptide consisting of 3 to 20 amino acid residues, or a peptidomimetic analog thereof wherein the analog is at least partly non-peptide in nature and the analog has a length equiv. to that detd. by 3 to 20 amino acid residues; which is a sequence not naturally occurring in the native sequence of the HSV-2 gG **protein**; and which has the following sequence SEQ ID:1 (X)n-.alpha.-.beta.-.gamma.-(Y)m or SEQ ID:2 (X)n-.delta.-.epsilon.-.phi.-(Y)m wherein n=0 or an integer; m=0 or an integer; n+m.ltoreq.17; .alpha. is E or may be substituted in order of preference by D>T>S>Q>N; .beta. is H; .gamma. is R or may be substituted in order of preference by R>A or L>T or P; .delta. is T or may be substituted in order of preference by E>L; .epsilon. is P; .phi. is L or may be substituted in order of preference by B or Y; and X or Y are **pos. charged**, **neg. charged** or neutral amino acids or peptidomimetic analogs thereof; and antibodies raised thereto; and prophylactic and therapeutic and diagnostic uses thereof relating to HSV-2 **infection**. Recombinant DNA encoding these peptides and vaccine compn. contg. the peptide and immune **adjuvant** or **carrier** are also disclosed.

L16 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	1997:775527 CAPLUS
DOCUMENT NUMBER:	128:66384
TITLE:	**Positively charged** liposome functions as an efficient immunoadjuvant in inducing immune responses to soluble **proteins**
AUTHOR(S):	Nakanishi, Tsuyoshi; Kunisawa, Jun; Hayashi, Akira; Tsutsumi, Yasuo; Kubo, Kazuyoshi; Nakagawa, Shinkasu; Fujiwara, Hiromi; Hamaoka, Toshiyuki; Mayumi, Tadanori
CORPORATE SOURCE:	Faculty and Graduate School of Pharmaceutical Science, Osaka University, Suita, 565, Japan
SOURCE:	Biochem. Biophys. Res. Commun. (1997), 240(3), 793-797 CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER:	Academic Press
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB To design an optimum liposome immunoadjuvant for sol. **protein antigens**, the authors investigated the

relationship between liposomal surface **charge** and **adjuvant** action. **P s. charged** multilamellar vesicles (MLV) were taken up efficiently by macrophages, while **neg. charged** and neutral MLVs were hardly picked up. Consistent with this, **pos. charged** MLVs contg. sol. chicken egg albumin (OVA) functioned as a more potent inducer of **antigen**-specific **cytotoxic T lymphocyte** (CTL) responses and antibody prodn. than **neg. charged** and neutral MLVs contg. the same concns. of **antigens**. The **pos. charge** on the surface of liposomes represents an important factor for enhancing their immunoadjuvancy in the induction of **antigen**-specific immune responses.

L16 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:738548 CAPLUS
DOCUMENT NUMBER: 128:72153
TITLE: Interactions of a tetravalent branched peptide from VP3 capsid **protein** of **hepatitis** A virus with monolayers as biomembrane models
AUTHOR(S): Alsina, Asuncion; Perez, Jose Antonio; Garcia, Monica; Reig, Francisca; Haro, Isabel
CORPORATE SOURCE: Physicochemical Unit, Faculty of Pharmacy, University of Barcelona, Barcelona, 08028, Spain
SOURCE: Supramol. Sci. (1997), 4(3-4), 195-199
CODEN: SUSCFX; ISSN: 0968-5677
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The interactions between a synthetic multiple antigenic peptide contg. four units of a peptide corresponding to the sequence (110-121) of VP3 **protein** of the **hepatitis** A virus, termed MAP4-VP3(110-121), and **phospholipids** as the main components of biol. membranes have been studied in detail. Surface activity of the multiple antigenic peptide was detd. as a function of its bulk concn. in an aq. soln. Satn. was reached at 0.33 .mu.M concn. The ability of the peptide to insert into lipid monolayers of dipalmitoyl phosphatidylcholine, dipalmitoyl phosphatidylglycerol and stearyl amine was detd. The peptide interacts preferably with the **pos. phospholipid** according to its **neg. charge**.

L16 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:623071 CAPLUS
DOCUMENT NUMBER: 127:298739
TITLE: Delivery of nucleic acids by porphyrins
INVENTOR(S): Takle, Garry B.; George, Shaji T.

PATENT ASSIGNEE(S): Innovir Laboratories, Inc., USA; Takle, Garry B.; George, Shaji T.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9733622	A2	19970918	WO 1997-US4000	19970314
WO 9733622	A3	19980226		
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9723244	A1	19971001	AU 1997-23244	19970314
EP 894011	A2	19990203	EP 1997-915946	19970314
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1996-616141 19960314
WO 1997-US4000 19970314

AB Efficient methods and compns. are provided for the targeted delivery of effective concns. of compds., including nucleic acid mols. and oligonucleotides such as external guide sequences for RNase P, ribozymes, antisense oligonucleotides, **proteins**, peptides, carbohydrates, and synthetic org. and inorg. mols., or combinations thereof, to cells, esp. hepatocytes, for diagnostic or therapeutic use. In the preferred embodiment, the compd. is a **neg. charged** oligonucleotide which binds in a stoichiometric ratio to a water-sol., **pos. charged** macrocyclic compd. such as a porphyrin, which targets and protects the oligonucleotide. In another embodiment, the porphyrin has anti-**human hepatitis virus** activity when administered alone; this activity is enhanced when the porphyrin is combined with an antiviral compd., esp. an oligonucleotide. Thus, binding of an oligoribonucleotide by meso-tetra(N-methyl-4-pyridyl)porphine tetratosylate (TMP) protected it from degrdn. by serum nucleases. Uptake of an oligodeoxyribonucleotide by human hepatoma cells was promoted by binding to TMP.

L16 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:337681 CAPLUS
DOCUMENT NUMBER: 127:16279
TITLE: Antiphospholipid antibodies: basic immunology and assays
AUTHOR(S): Schultz, Duane R.
CORPORATE SOURCE: Department of Medicine, University of Miami

School of Medicine, Miami, FL, 33101, USA
SOURCE: Semin. Arthritis Rheum. (1997), 26(5), 724-739
CODEN: SAHRBF; ISSN: 0049-0172
PUBLISHER: Saunders
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 122 refs. Great progress has been made within the past 10 yr in characterizing, assaying, and describing mechanism(s) of action in vitro of antiphospholipid antibodies (a-PL Abs); three prominent members are reagin, anticardiolipin antibodies (a-CL Abs), and the lupus anticoagulants (LAC). The major focus of this review is on basic and current biochem. and immunol. research. First, the biochem., structural compn., and sources of anionic and dipolar ionic (zwitterionic) **phospholipids** are discussed together with several serum antibodies directed to these **phospholipids**. **Cardiolipin**, the most acidic **phospholipid** (net **neg. charge** of 2 at pH 7.0) has been historically important as an **antigen** for testing reagin in syphilis serol., and currently is part of the antigenic compn. used in the Venereal Disease Research Lab. (VDRL) tests. In this connection, the chronic biol. false-**pos**. test for syphilis and the LAC are discussed in assocn. with autoimmune disorders such as systemic lupus erythematosus. Second, a naturally occurring plasma anticoagulant in vitro and a crit. cofactor for binding of purified autoimmune a-CL Abs to **cardiolipin** is considered, the .beta.2-glycoprotein I (.beta.2-gpI). This single-chain plasma polypeptide is highly glycosylated, has 326 amino acids, a mol. wt. of 50 kD, and is characterized by repeating amino acid motifs or domains that structurally resemble multiple loops. The highly cationic C-terminal fifth domain binds to anionic **phospholipids**. The .beta.2-gpI is a member of the short consensus repeat superfamily of **proteins**, and is compared with other **proteins** with similar domains. Third, expts. are detailed for defining LAC and distinguishing it from other a-CL Abs. Cofactors are also assocd. with LAC and include .beta.2-gpI, prothrombin, **protein** C, **protein** S, tissue factor, and factor XI. Thus, LAC antibodies are heterogeneous, and no individual assay can detect all LACs. Because patients with syphilis and other infectious diseases have no cofactor assocd. with a-CL Abs, their plasma LACs are **neg**. The a-CL Abs found in **infection** are not assocd. with the clin. features of the antiphospholipid syndrome. LAC assays are important because of the pathogenetic assocn. with clin. observations of venous and arterial thrombosis, thrombocytopenia, and recurrent fetal loss. Finally, reports leading to development of currently used direct solid-phase enzyme-linked immunosorbent assays (ELISA) for testing a-PL Abs are outlined; these developments have greatly increased

understanding of the basic immunol. of target **antigens** and their resp. antibodies. Of significance, a-CL Abs cross-react with other anionic **phospholipids**. Addnl., the results of these assays led to the realization that high levels of circulating a-PL Abs over long periods are assocd. with a no. of clin. problems now known collectively as the antiphospholipid syndrome.

L16 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:739359 CAPLUS
DOCUMENT NUMBER: 123:160171
TITLE: Protective effect of Brucella outer membrane complex-bearing liposomes against experimental murine brucellosis
AUTHOR(S): Vitas, Ana I.; Diaz, Ramon; Gamazo, Carlos
CORPORATE SOURCE: Dpto. de Microbiologia, Universidad de Navarra, Pamplona, 31080, Spain
SOURCE: FEMS Microbiol. Lett. (1995), 130(2-3), 231-6
CODEN: FMLED7; ISSN: 0378-1097
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Liposomes of stable multilamellar type, which previously demonstrated great efficiency in antibiotic transport, were used in this study as transport vehicles of antigenic exts. of Brucella melitensis (HS: complex of lipopolysaccharide/**phospholipids** /outer membrane **proteins**). The incorporation of HS into **pos. charged** liposomes produced a protective effect against exptl. murine brucellosis when they were administered 1 day before or 2 days after **infection**, as the no. of colony-forming units in the spleen was reduced in relation to the untreated control group. The use of HS-free or bound in liposomes with **neg.** net **charge** did not produce a significant effect. Moreover, the incorporation of HS into cationic liposomes eliminated the toxicity of the lipopolysaccharide.

L16 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:678717 CAPLUS
DOCUMENT NUMBER: 121:278717
TITLE: An amphipathic peptide from the C-terminal region of the **human** immunodeficiency **virus** envelope glycoprotein causes pore formation in membranes
AUTHOR(S): Chernomordik, L.; Chanturiya, A. N.; Suss-Toby, E.; Nora, E.; Zimmerberg, J.
CORPORATE SOURCE: Lab. Theoretical, Physical Biol., National Inst. Child Health Human Dev., National Inst. Health, Bethesda, MD, 20892, USA
SOURCE: J. Virol. (1994), 68(11), 7115-23
CODEN: JOVIAM; ISSN: 0022-538X

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The peptide fragment of the carboxy-terminal region of the **human** immunodeficiency **virus** (**HIV**) transmembrane **protein** (gp41) has been implicated in T-cell death. This **pos. charged**, amphipathic helix (amino acids 828 to 848) of the envelope **protein** is located within virions or cytoplasm. We studied the interaction of the isolated, synthetic amphipathic helix of gp41 with planar **phospholipid** bilayer membranes and with Sf9 cells using voltage clamp, potentiodynamic, and single-cell recording techniques. We found that the peptide binds strongly to planar membranes, esp. to the **neg. charged** phosphatidylserine bilayer. In the presence of micromolar concns. of peptide sufficient to make its surface densities comparable with those of envelope glycoprotein mols. in **HIV** virions, an increase in bilayer conductance and a decrease in bilayer stability were obsd., showing pore formation in the planar lipid bilayers. These pores were permeable to both monovalent and divalent cations, as well as to chloride. The exposure of the inner leaflet of cell membranes to even 25 nM peptide increased membrane conductance. We suggest that the carboxy-terminal fragment of the **HIV** type 1 envelope **protein** may interact with the cell membrane of infected T cells to create lipidic pores which increase membrane permeability, leading to sodium and calcium flux into cells, osmotic swelling, and T-cell necrosis or apoptosis.

L16 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:75477 CAPLUS
DOCUMENT NUMBER: 118:75477
TITLE: **Carrier**-mediated transport of tetrabromosulfonephthalein by rat liver plasma membrane vesicles
AUTHOR(S): Torres, Adriana M.; Rodriguez, Joaquin V.; Lunazzi, Gian Carlo; Tiribelli, Claudio
CORPORATE SOURCE: Cent. Stud. Fegato, Univ. Trieste, Trieste, 34100, Italy
SOURCE: Am. J. Physiol. (1992), 263(3, Pt. 1), G338-G344
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To examine the mol. requirements and mechanisms for the hepatic uptake of phthaleins, the transport of tetrabromosulfonephthalein (**TBS**) was investigated in basolateral rat liver plasma membrane vesicles. **TBS** uptake was electrogenic as greatly accelerated by the creation of a **pos.**-inside membrane potential by the addn. of valinomycin in the presence of an inwardly directed potassium gradient. No effect was obsd. when the ionophore

was added in the presence of a sodium gradient. The transport occurred into an osmotic-sensitive space and was saturable with an apparent Michaelis const. of 5.32 .mu.M and a maximal velocity of 9.23 nmol/s/mg **protein**. **TBS** uptake was directly related to the extravesicular pH, indicating the deprotonated quinoid **neg.-charged** form of the dye as the transported species. In contrast, **TBS** uptake was inversely related to the intravesicular pH, suggesting that protonation inside the vesicles may act as an efficient trap in transport process. Addn. of polyclonal monospecific anti-bilitranslocase antibody to liver vesicles specifically inhibited **TBS** uptake rate (3.27 vs. 5.82 nmol/s/mg **protein**). Thus, **TBS** is electrogenically transported across the liver cell plasma membrane by bilitranslocase. Furthermore, the presence of a **neg. charged** group on the benzenic ring of the ligand is important in accounting for the transport.

L16 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:445810 CAPLUS
DOCUMENT NUMBER: 115:45810
TITLE: Interaction of non-enveloped plant viruses and their viral coat **proteins** with **phospholipid** vesicles
AUTHOR(S): Spruijt, Ruud B.; Boehmer, Marcel R.; Wilschut, Jan; Hemminga, Marcus A.
CORPORATE SOURCE: Dep. Mol. Phys., Agric. Univ., Wageningen, 6703 HA, Neth.
SOURCE: Biochim. Biophys. Acta (1991), 1065(2), 217-24
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The interaction of the non-enveloped plant viruses TMV (rod-shaped) and CCMV (spherical) and of their coat **proteins**, in several well-defined aggregation states, with artificial membranes was investigated to study the early stages of the cellular **infection** process. Information about the sep. steps in the interaction mechanisms was obtained by employing three assays, performed as a function of vesicle size, net membrane **charge**, pH and ionic strength. The assays allow to discriminate between aggregation of vesicles (turbidity assay) and membrane destabilization (vesicle leakage assay and lipid mixing assay). The aggregation of the vesicles is a result of electrostatic interactions between the viral material and vesicles surface (crosslinking), while the destabilization of the membrane is a result of penetration or bilayer disruption by hydrophobic **protein** domains. TMV virions and its coat **protein**, and CCMV virions, due to their net **neg. charge**

, predominantly interact with **pos. charged** membranes. The coat **protein** of CCMV was found to interact with **neg. charged** membranes, an interaction that can be assigned to its basic N-terminal sequence. Changing the aggregational state of the viral coat **proteins** yielded most significant interactions in the case of TMV coat **protein** aggregated in the disk form and CCMV coat **protein** aggregated in empty capsids with oppositely **charged** membranes. These **protein** aggregates are found to be the best compromise between efficiency (capacity of the **protein** to bridge vesicles and destabilize their membranes) and concn. of **protein** aggregates. The results are discussed with respect to previously proposed biol. models of the early stages of plant virus **infection**.

L16 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1972:445140 CAPLUS
DOCUMENT NUMBER: 77:45140
TITLE: Experimental basis for serological diagnosis of **tuberculosis** using nycobacterial **phospholipid antigens**
AUTHOR(S): Motomiya, Masakichi; Takeda, Shumpei; Kobayashi, Tatsuo; Oka, Sutemi
CORPORATE SOURCE: Res. Inst. Tuberc. Leprosy Cancer, Tohoku Univ., Sendai, Japan
SOURCE: Sci. Rep. Res. Inst., Tohoku Univ., Ser. C (1971), 18(1-2), 22-6
CODEN: SRTCAC
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Earlier work had shown that **phospholipids** (PL) isolated from the cell wall of mycobacteria reacted as an **antigen** (Ag) with mycobacterial antisera (Ab). In order to test the sensitivity and specificity of the immunol. reaction, various different PL structures were tested against various different Ab prepd. from the microbes that commonly cause respiratory **infections**. PL-coated latex particles were incubated with dilns. of Ab, and reactivity was indicated by agglutination of the particles. The type of PL, not its source, detd. whether or not agglutination took place. The absence of reaction with phosphatidylcholine suggested that a **pos. charge** on the PL interfered with the Ag-Ab reaction. The disappearance of reactivity with **phosphatidylinositol** (PI) monomannoside (M) after acetylation along with a **neg.** reaction with PI, suggested that the M moiety was essential for the Ab-Ag reaction. Phosphatidylethanol-amine-coated particles were agglutinated by Ab against P seudomonas, Staphylococcus, and Streptococcus as well as mycobacteria. PIM-coated particles were agglutinated only with

mycobacterial Ab and showed agglutination at high diln. of Ab, indicating that this PL-Ag had both high sensitivity and specificity in an immunol. test for mycobacteria.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, CANCERLIT' ENTERED AT 14:33:06 ON 24 APR 2001)

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L17          12 S L14
L18          89 S L15
L19          18 S L18 AND (TREAT? OR THERAP? OR PROPHYL?)
L20          29 S L17 OR L19
L21          21 DUP REM L20 (8 DUPLICATES REMOVED)
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L21 ANSWER 1 OF 21 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2001-112443 [12] WPIDS
DOC. NO. CPI: C2001-033472
TITLE: New peptides and its encoding nucleic acid derived from intestinal carboxyesterase, useful as immunostimulants for treating cancer.
DERWENT CLASS: B04 D16
INVENTOR(S): RONSIN, C; SCOTT, V; TRIEBEL, F
PATENT ASSIGNEE(S): (INSR) INST ROUSSY GUSTAVE
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001000784	A2	20010104	(200112)*	FR	52

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

FR 2795415 A1 20001229 (200112)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001000784	A2	WO 2000-FR1791	20000627
FR 2795415	A1	FR 1999-8224	19990628

PRIORITY APPLN. INFO: FR 1999-8224 19990628
AN 2001-112443 [12] WPIDS
AB WO 200100784 A UPAB: 20010302
NOVELTY - A peptide (I) containing at least 8 consecutive amino

acids (aa) from a 162 aa sequence (S1) fully defined in the specification and able to induce a T-specific response, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) identifying (M1) peptides (1a) at least 80% identical with a sequence of 9 or 10 contiguous aa of (S1);

(2) (Ia) identified by (M1);

(3) detecting (M2) mutations and artificial point alterations that increase the immunogenicity of (I) and (Ia);

(4) a peptide (Ib) identified by (M2) with a sequence of 9 or 10 aa from (S1) and at least one mutation relative to (S1), able to induce a T-specific response;

(5) a DNA fragment (II) encoding at least one (I), (Ia) or (Ib);

(6) a vector for expressing (I), (Ia) or (Ib) that contains (II) fused to a promoter functional in eukaryotic and/or prokaryotic, particularly human, cells;

(7) dendritic cells (DC) loaded with (I), (Ia) or (Ib), or their mixtures, or transformed with the vector of (6);

(8) a pharmaceutical composition containing any of (I), (Ia), (Ib), or their mixtures, the vector of (6), (II) or the cells of (7);

(9) preparing monoclonal antibodies (MAb) that recognize (I), (Ia) or (Ib);

(10) MAb immunospecific for (I), (Ia) or (Ib);

(11) detecting a (poly) peptide encoded by the displaced open reading frame (ORF+1) of the iCE (intestinal carboxyesterase) gene;

(12) a diagnostic kit containing MAb for detection and prognosis of cancer; and

(13) a pharmaceutical composition containing MAb and a **carrier**.

ACTIVITY - Anticancer; immunostimulant.

MECHANISM OF ACTION - (I) induce tumor-specific **cytotoxic T lymphocytes** (CTL) and secretion by these CTL of **cytotoxic** factors, e.g. interleukin-2, interferon gamma and tumor necrosis factor. No supporting data given.

USE - (I), related peptides, DNA (II) that encodes them, vectors containing (II) and cells containing the vectors, are used:

(1) for treating cancer, by in vivo or in vitro immunization, particularly solid cancers and most especially hepatocarcinoma or adenocarcinoma of colon and kidney;

(2) to stimulate the immune system; and

(3) to increase, in culture, the production of tumor-associated **cytotoxic T lymphocytes** (CTL), for reinjection, and/or to induce secretion of **cytotoxic** factors from CTL.

Dendritic cells loaded with (I) are used to induce such CTL in

cultures, and antibodies raised against (I) may be used therapeutically or to detect peptides encoded by the alternative open reading frame of the human iCE (intestinal carboxyesterase) gene, especially for diagnosis and prognosis of cancer.
Dwg.0/8

L21 ANSWER 2 OF 21 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-656212 [63] WPIDS
DOC. NO. CPI: C2000-198616
TITLE: Immunomodulating polymers, useful for **treating** interleukin-2 (IL-2)-responsive (e.g. **melanoma**) or T-cell-responsive (e.g. inflammatory bowel disease or allograft rejection) disorders, or protecting against abscess formation.
DERWENT CLASS: B04 B05 D16
INVENTOR(S): KASPER, D L; ONDERDONK, A B; TZIANABOS, A O; WANG, Y
PATENT ASSIGNEE(S): (BGHM) BRIGHAM & WOMENS HOSPITAL INC
COUNTRY COUNT: 86
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000059515	A2	20001012	(200063)*	EN	99
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW					
AU 2000040563	A	20001023	(200107)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000059515	A2	WO 2000-US8586	20000331
AU 2000040563	A	AU 2000-40563	20000331

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000040563	A Based on	WO 200059515

PRIORITY APPLN. INFO: US 1999-162457 19991029; US 1999-127584 19990402

Searcher : Shears 308-4994

AN 2000-656212 [63] WPIDS
AB WO 200059515 A UPAB: 20001205
NOVELTY - A composition comprising a polymer or polypeptide of less than 50 kilodaltons (kDa) having at least 2 repeating **charge** motifs and a **carrier**, is new.

DETAILED DESCRIPTION - A composition comprising a polymer or polypeptide of less than 50 kilodaltons (kDa) having at least 2 repeating **charge** motifs and a **carrier**, is new. The repeating **charge** motif is composed of a **positively charged** free amino group and a **negative charge**. The **positively charged** free amino groups of the two repeating **charge** motifs of the polymer or polypeptide are separated by a neutral intervening sequence of at least 32 Angstrom or 8 amino acids.

INDEPENDENT CLAIMS are also included for the following:

(1) methods of inducing IL-2 secretion comprising contacting an IL-2-secreting cell with the polymer or polypeptide;

(2) a method of **treating** an IL-2-responsive disorder by inducing IL-2 secretion comprising administering the polymer;

(3) methods for inducing protection against abscess formation associated with **infection** comprising administering to a subject a pharmaceutical preparation containing an IL-2 or an IL-2 inducing compound, the polymer or polypeptide;

(4) methods of activating T cells comprising contacting a T cell in the presence of an **antigen** presenting cell with the polymer or polypeptide;

(5) a method for **treating** a T-cell-responsive disorder by activating a T cell to produce Th1-cell-specific cytokines comprising administering the polymer to a subject who is not preparing to undergo surgery, thus inducing IL-2 secretion by the T cell;

(6) a method for **treating** a subject having a disorder characterized by an inappropriate IgG (immunoglobulin G) antibody response to a specific **antigen** comprising administering the polymer to a subject who is not preparing to undergo surgery, where the polymer is a polypeptide and does not consist of lysine (K), glutamic acid (E), alanine (A) or tyrosine (Y) residues in a relative molar ration of 3-7 parts of K to 1-3 parts of E to 4-7 parts of A to 0.5-2 parts of Y; and

(7) methods for reducing postoperative surgical adhesion formation occurring at a surgical site comprising administering the pharmaceutical preparation at a site other than at the surgical site, where the preparation produces protection against postoperative surgical adhesion formation of a zwitterionic non-polysaccharide or polysaccharide polymer having at least 2 repeating **charge** units.

ACTIVITY - Antiinflammatory; antibacterial; immunomodulator;

cytostatic; antidiabetic; anti-**human** immunodeficiency **virus** (**HIV**); neuroprotective.

MECHANISM OF ACTION - T cell activator; interleukin-2 stimulator; interleukin-10 stimulator; IgG antibody response suppressor.

SVJ mice were **treated** on day 0 with 50 mu g of polysaccharide A (PS A) via the intraperitoneal route and 2 mu g of a conjugate vaccine containing type III group B Streptococcus polysaccharide and tetanus toxoid. Controls received saline in place of PS A. **Antigen**-specific IgG levels were assayed by sandwich ELISA (enzyme linked immunosorbent assay), using a specific **antigen** as the capture agent. ELISA testing of antibody levels showed that the levels of IgG specific for the type III polysaccharide in PS A-**treated** animals were suppressed compared to saline-**treated** animals. Thus, PS A **treatment** suppressed IgG response to both polysaccharide and peptide **antigens**.

USE - The composition is useful for inducing IL-2 secretion or **treating** an IL-2-responsive disorder, e.g. **acquired** immune deficiency **syndrome** (**AIDS**), renal cell carcinoma or **melanoma**. The composition is also useful for inducing IL-2 or IL-10, which is particularly useful for inducing protection against abscess formation associated with **infection**. Protection against abscess formation may also be induced by administering IL-2, or an IL-2-inducing compound, e.g. an activated T cell, staphylococcal enterotoxin A (SEA), an anti-CD3 antibody, an oxidative chemical or tucaresol (4(2-formyl-3-hydroxyphenoxymethyl) benzoic acid). The composition may be administered before or after the patient has been exposed to abscess forming conditions. It may also be administered to a subject who has undergone or is in need of surgery. Furthermore, the composition is useful for activating a T cell to produce Th1-cell-specific cytokines for **treating** a T-cell-responsive disorder in a subject who is not preparing to undergo surgery. The T-cell-responsive disorder includes insulin-dependent diabetes mellitus, experimental allergic encephalomyelitis, inflammatory bowel disease, or allograft rejection. Furthermore, the composition is useful for activating T cells and for **treating** a T-cell-responsive disorder. The composition may also be used for **treating** a subject having a disorder characterized by an inappropriate IgG antibody response to a specific **antigen** in a subject who is not preparing to undergo surgery. The composition is also useful for reducing postoperative surgical adhesion formation occurring at a surgical site.

Dwg.0/1

L21 ANSWER 3 OF 21 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-571930 [53] WPIDS

DOC. NO. CPI: C2000-170417
TITLE: Immunogenic complexes comprising **negatively charged** organic **carrier adjuvants** and **positively charged antigens** for use as vaccines against microbial **infection** and cancer.
DERWENT CLASS: B04 D16
INVENTOR(S): COX, J C; DRANE, D P
PATENT ASSIGNEE(S): (CSLC-N) CSL LTD
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000048630	A1	20000824	(200053)*	EN	111

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000026515	A	20000904	(200103)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000048630	A1	WO 2000-AU110	20000217
AU 2000026515	A	AU 2000-26515	20000217

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000026515	A	Based on	WO 200048630

PRIORITY APPLN. INFO: AU 1999-1861 19990727; AU 1999-8735 19990217
AN 2000-571930 [53] WPIDS
AB WO 200048630 A UPAB: 20001023
NOVELTY - An immunogenic complex comprising a **charged** organic **carrier** and a **charged antigen** which are electrostatically associated, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a vaccine composition comprising as the active component a complex as above, together with one or more **carriers**

and/or diluents;

(2) eliciting, inducing or otherwise facilitating, in a mammal, an immune response to an **antigen**, comprising administering to the mammal an effective amount of the novel complex or the vaccine of (1); and

(3) an agent for inhibiting, halting, delaying or preventing the onset or progression of a disease or condition, comprising the novel complex or the vaccine of (1).

ACTIVITY - Virucide; Hepatropic; Antiinflammatory; **Tuberculostatic**; Cytostatic. No biological data is given.

MECHANISM OF ACTION - Immunogenic complex; Vaccine.

USE - The complex induces a **cytotoxic T lymphocyte** (CTL) response. The complex and/or vaccine can be used to **treat** a disease in a mammal, where the complex/vaccine elicits, induces or otherwise facilitates an immune response which inhibits, halts, delays or prevents the onset or progression of the disease condition. In particular, the disease is a condition resulting form a microbial **infection** or cancer. Microbial **infections** include **human** immunodeficiency **virus (HIV)**, **hepatitis** B, **hepatitis** C, **tuberculosis** or a **parasitic condition** and the cancer is **melanoma**, prostate cancer or breast cancer. All claimed.

ADVANTAGE - The complexes and vaccines co-deliver **antigen** and **adjuvant** at the same time to the same **antigen** presenting cell, which is often essential for induction of appropriate immune responses.

Dwg.0/15

L21 ANSWER 4 OF 21 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-224340 [19] WPIDS
DOC. NO. CPI: C2000-068509
TITLE: New recombinant retrovirus for **treating** or preventing retroviral **infection** including **human** immunodeficiency **virus (HIV)**-1, has a modified or replaced virus envelope glycoprotein natural signal sequence.
DERWENT CLASS: B04 D16
INVENTOR(S): KANG, C; LI, Y
PATENT ASSIGNEE(S): (UYWO-N) UNIV WESTERN ONTARIO
COUNTRY COUNT: 88
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000009703	A1	20000224	(200019)*	EN	26

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC

MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM
EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD
SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9952740 A 20000306 (200030)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000009703	A1	WO 1999-CA746	19990812
AU 9952740	A	AU 1999-52740	19990812

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9952740	A	Based on	WO 200009703

PRIORITY APPLN. INFO: US 1998-96235 19980812
AN 2000-224340 [19] WPIDS
AB WO 200009703 A UPAB: 20000419
NOVELTY - A non-cytolytic recombinant virus where the natural signal sequence (NSS) of the virus envelope glycoprotein is replaced with an essentially non-cytolytic signal sequence, or is modified to provide an essentially non-cytolytic sequence, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a non-cytolytic recombinant retrovirus where the NSS of the virus' envelope glycoprotein is modified to provide an essentially non-cytolytic signal sequence;

(2) a vaccine incorporating the novel retrovirus or the retrovirus of (1);

(3) a method of preventing or **treating** a retroviral **infection**, comprising administering an essentially non-cytolytic recombinant retrovirus, where the NSS of the virus' envelope glycoprotein is replaced with an essentially non-cytolytic NSS and the retrovirus is rendered avirulent;

(4) a method of preventing or **treating** a retroviral **infection** comprising administering to an animal, an essentially non-cytolytic recombinant retrovirus where the NSS of the virus envelope glycoprotein is modified to provide a non-cytolytic NSS;

(5) a vaccine comprising an essentially non-cytolytic recombinant retrovirus where the NSS of the virus' envelope glycoprotein is replaced with an essentially non-cytolytic NSS;

(6) a vaccine comprising an essentially non-cytolytic

recombinant retrovirus where the NSS of the retrovirus envelope glycoprotein is modified to provide an essentially non-cytolytic NSS and the retrovirus is rendered avirulent;

(7) a method of killing a target cell, comprising administering a recombinant virus containing NSS and a recognition site specific to the cell; and

(8) a method of inhibiting the effects of the NSS of a retrovirus, comprising administering an antisense oligonucleotide that is complementary to a nucleic acid sequence for an NSS **protein** gene to an animal

ACTIVITY - Virucide.

MECHANISM OF ACTION - Vaccine.

USE - The recombinant virus is used as a vaccine to prevent or **treat** a retroviral **infection**, especially a **HIV infection** (claimed).

ADVANTAGE - Unlike prior art, where avirulence has resulted in low replication, the invention provides a vaccine that is both avirulent and capable of being produced in large quantities.

Dwg.2/12

L21 ANSWER 5 OF 21 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000-410878 [35] WPIDS

CROSS REFERENCE: 1997-470878 [43]

DOC. NO. CPI: C2000-124450

TITLE: New molecular complex having a gene encoding an interferon linked to a nucleic acid binding agent and a ligand that binds to a cell receptor, useful for targeted delivery of the genes in **treating** diseases responsive to interferon **therapy**.

DERWENT CLASS: B04 D16

INVENTOR(S): CARLO, D J; CHIOU, H C

PATENT ASSIGNEE(S): (IMMU-N) IMMUNE RESPONSE CORP

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6069133	A	20000530	(200035)*		28

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6069133	A	CIP of	US 1996-616023	19960314
			US 1997-819238	19970317

PRIORITY APPLN. INFO: US 1997-819238 19970317; US 1996-616023 19960314
AN 2000-410878 [35] WPIDS
CR 1997-470878 [43]
AB US 6069133 A UPAB: 20000725
NOVELTY - A molecular complex comprising a gene encoding an interferon (IFN) releasably linked to a conjugate of a cationic agent that binds the gene and a ligand that binds to an asialoglycoprotein receptor on liver cells, is new.

DETAILED DESCRIPTION - A molecular complex comprising a gene encoding an interferon (IFN) releasably linked to a conjugate of a cationic agent that binds the gene and a ligand that binds to an asialoglycoprotein receptor on liver cells, is new. The gene is operably linked to the thyroxin binding globulin (TBG) promoter, and one or more copies of the alpha-1 microglobulin/bikunin (ABP) enhancer, such that the gene is expressed, processed and secreted from the target cell.

An INDEPENDENT CLAIM is also included for a method of delivering a gene encoding IFN to a target liver cell in a mammal comprising administering to the mammal the molecular complex.

ACTIVITY - Immunomodulator; cytostatic; hepatotropic; antiinflammatory; anti-**human** immunodeficiency **virus** (**HIV**).

MECHANISM OF ACTION - Gene **therapy**; interferon agonist. A 1.0 ml dose of complex solution (pJ7 Omega IFN alpha -P1-ASOR, pJ7 Omega hIFN alpha -P1-ASOR, pJ Omega hIFN alpha SB-P1-ASOR, pJ7 Omega hIFN alpha -nonSB-P1-ASOR, pSVIFN alpha -P1-ASOR and pSVIFN alpha RV-P1-ASOR) was injected into adult female BALB/C mice. Additional control mice received 1.0 ml injections of an identically formulated human growth hormone (hGH) plasmid-containing complex. Blood samples were taken from the animals and serum from samples were analyzed for human IFN- alpha 2b **protein** by ELISA (enzyme linked immunosorbent assay). Control animals **treated** with hGH complex did not produce any measurable human IFN- alpha 2b. Animals **treated** with the complex solution showed long-term in vivo expression of IFN.

USE - The molecular complex is useful for targeted delivery of genes encoding IFN to selected cells. The molecular complex can be delivered to selected cells in vivo to **treat** a variety of diseases that are responsive to IFN **therapy**. Alternatively, the molecular complex can be delivered to selected cells in vitro to produce recombinant IFN which can be administered as exogenous **protein** to patients in conventional IFN **protein therapy**. IFN is useful in **treating** hairy cell leukemia, condyloma, Kaposi's sarcoma in **AIDS** (**acquired** immune deficiency **syndrome**) patients or type C **hepatitis infection**.

ADVANTAGE - IFN **therapy** currently involves

administration of exogenous IFN to patients on a frequent (e.g. daily) basis. High dosages are often required to achieve a sufficient concentration of IFN in target tissues. In addition, patients often experience a variety of adverse side effects and/or peripheral toxicities associated with systemic delivery of IFN. The molecular complex provides an improved form of IFN replacement **therapy**. The process employs targeted delivery of genes encoding IFN, therefore it requires a smaller dose and has low toxicity.
Dwg.0/17

L21 ANSWER 6 OF 21 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-205219 [18] WPIDS
DOC. NO. CPI: C2000-063189
TITLE: Cephalosporin derivatives as beta-lactam anitbiotics, useful in the **treatment** of **infection** by bacteria resistant to vancomycin, methicillin, imipenem.
DERWENT CLASS: B02
INVENTOR(S): CHO, I; GLINKA, T W; HECKER, S J; LEE, V J; ZHANG, Z J
PATENT ASSIGNEE(S): (MICR-N) MICROCIDE PHARM INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6030965	A	20000229	(200018)*		41

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6030965	A	US 1997-940508	19970930

PRIORITY APPLN. INFO: US 1997-940508 19970930
AN 2000-205219 [18] WPIDS
AB US 6030965 A UPAB: 20000412
NOVELTY - Cephalosporin derivatives (I) and their salts, are new
DETAILED DESCRIPTION - Cephalosporin derivatives of formula (I) and their salts are new.
R1 = NHC(O)Z'R3, NR4R5 or a group of formula (i);
Z' = CH2(X)m, C(=NOR6), CH(OR7), C(CHCO2R8) or CH(NR9R10);
X = O or S;
m = 0 - 1;
R3 = CN, alkyl (optionally substituted with Q'), aryl (optionally substituted with Q), Het (optionally substituted with Q

or oxo) or (CH2)nT;

Q = OH, Br, F, Cl, I, SH, CN, alkylthio, carboxyl, alkoxycarbonyl, alkenyl, nitro, amino, alkoxyl, or carboxamido;

Q' = Q, isothioureido, amidino or guanidino;

Het = furyl, thienyl, imidazilyl, indolyl, pyridinyl, thiadiazolyl, thiazolyl, piperazinyl, dibenzfuranyl, dibenzthienyl, pyrimidinyl or pyridazinyl;

n = 1 - 6

T = amino, C- or N- linked amidino, guanidino, or isothioureido, optionally substituted by alkyl, aryl, hydroxyl or amino;

R4 - R8 = H, acyl, alkyl (optionally substituted by Q') or aryl (optionally substituted by Q);

R9, R10 = H, alkyl (optionally substituted with Q'), acyl or heterocyclylcarbonyl (optionally substituted with Q or oxo);

R12 = NR13R14, C(=N+R13R14)NR15R16, NR13C(=NR14)NR15R16, NR13C(=NR14)R17, or SC(=N+R13R14)NR15R16;

R2 = H, alkyl (optionally substituted with Q'),alkenyl (optionally substituted with Q'), aryl (optionally substituted with Q), Het (optionally substituted with Q or oxo), aralkyl (optionally substituted on aryl portion with Q), heteroaralkyl (optionally substituted with Q or oxo) or trialkylsilyl; or when R12 is a cationic group, R2 is not present and the CO2 group to which it would be attached bears a **negative charge**);

A, B, D, E = C, N or S such that they form a heterocylic group selected from pyrrole, pyrazole, imidazole, 1,2,4-triazole, 1,2,3-triazole, 1,2,3,4-tetrazole, 1,2,3-thiadiazole, 2,1,3-thiadiazole, 1,3,4-thiadiazole, 1,2,4-thiadiazole or 1,3-thiazole;

R11 = H, halogen, alkyl (optionally substituted with Q''), alkoxy (optionally substituted with Q''), OH, amino, CN, hydroxyalkyl (optionally substituted with Q''), carboxxamidoalkyl (optionally substituted with Q'') or aminoalkyl (optionally substituted with Q'');

Q'' = Br, F, Cl, I, SH, CN, alkylthio, carboxyl, alkenyl, nitro, isothioureido, amidino or guanidino;

Alk1, Alk2 = alkylene optionally substituted with alklyl, hydroxylo, optionally substituted amino, alkoxy, hydroxyalkyl or optionally substituted carboxamide;

p = 0, 1, 2;

R99 = S, SO, SO2, NH, N-alkyl, O, C=C or C triple bond C;

q = 1;

r = 0 - 3;

s = 0 - 3;

t = 1 - 2; N.B. in a later dependent claim t = 1 - 4;

R13-R16 = H, OH, amino, amidino, alkyl (optionally substituted with Br, F, Cl, I, SH, CN, alkylthio, heterocycle, aryl, heteroaryl, nitro, alkoxyl, carboxamido, isothioureido, amidino or guanidino),

cycloalkyl, acyl, aminoacyl or phosphoryl; and

R17 = H or alkyl (optionally substituted with Br, F, Cl, I, SH, CN, alkylthio, heterocycle, aryl, heteroaryl, nitro, alkoxyl, carboxamido, isothioureido, amidino or guanidino).

INDEPENDENT CLAIMs are also provided for:

(1) a method of treating a mammal suffering from a methicillin resistant or ampicillin resistant bacterial infection comprising administration of (I); and

(2) an antibacterial composition comprising (I) in a carrier.

ACTIVITY - Antibacterial;

To determine the minimum inhibitory concentrations (MIC) for bacterial isolates, (7R)-7-((Z)-(aminothiazol-4-yl)-2-(hydroxyimino)acetamido)-3-((methylaminoethylaminoethylthiomethyl)-1,2,3-thiadiazol-5-ylthio)-3-cephem-4-carboxylate trifluoroacetate (Ia) was incorporated in a series of two-fold dilutions into liquified Muller-Hinton agar. Upon solidification a number of different bacterial strains were spot inoculated with a replicating device onto the agar surface. After overnight incubation the MIC breakpoint was determined as the lowest drug concentration that completely inhibited growth disregarding a single colony or a faint haze. The procedures used have been standardized by the National Committee for Clinical Laboratory Standards (NCCLS) as per the NCCLS publication entitled METHODS FOR DILUTION ANTIMICROBIAL SUSCEPTIBILITY TESTS (1991). Endpoints were assessed as the minimum inhibitory concentration (MIC) of antimicrobial agent. (Ia) had a MIC of 4 micro g/ml against S. aureus ATCC 33593 (MethR), against which imipenem had a MIC of 32 micro g/ml.

Groups of 5 female Swiss-Webster mice each are challenged by the intraperitoneal (IP) route with tenfold increments of a bacterial inoculum. This permits calculation of the mean lethal dose (LD50) and LD100. For preliminary evaluation of a new antibiotic, mice are challenged IP with an LD100 titer of bacteria. In two equal doses administered at the time of bacterial challenge and 2 hours later, groups of 10 mice each are treated subcutaneously with two-fold increments of the test drug and an antibiotic of known efficacy in mice and humans (i.e., positive control). Mice are observed for 72 hours. Those alive at 72 hours are considered long term survivors. The total drug dose in mg/kg that protects 50 % of mice in a group from death is termed the mean protective dose (PD50) . The PD50 is the same as the 50% effective dose (ED50). Against S. aureus ATCC 13709 (Ia) had an ED50 of 0.96 micro g/g whereas vancomycin had an ED50 of 1.94 micro g/g.

MECHANISM OF ACTION - Inhibitor of penicillin binding proteins.

USE - Used to treat infections by methicillin resistant Staphylococcal or ampicillin-resistant Enterococcal bacteria especially infection by S. Aureus Col (MethR)(lac-), S. aureus 76 (MethR)(lac+), S. aureus ATCC 33593 (MethR), S. aureus Spain No. 356 (MethR), S. haemolyticus 05 (MethR), E. faecalis ATCC 29212, E.

faecium ATCC 35667, E. Faecium VanA (VanR), E. faecalis Van B (VanR) or E. faecium A491 (AmpR) (claimed).

ADVANTAGE - The compounds are effective against pathogens resistant to beta -lactam antibiotics such as vancomyciin, methicillin, ampicillin and imipenem, allowing treatment of infections by these bacteria which are otherwise untreatable.

Dwg.0/5

L21 ANSWER 7 OF 21 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000-170661 [15] WPIDS
CROSS REFERENCE: 1999-008274 [01]
DOC. NO. CPI: C2000-052966
TITLE: Suppressing immune responses using non-immunogenic constructs free of high molecular weight immunostimulatory molecules.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): BLODGETT, J K; CHERONIS, J C; DINTZIS, H M; DINTZIS, R Z; KIRSCHENHEUTER, G
PATENT ASSIGNEE(S): (UYJO) UNIV JOHNS HOPKINS
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6022544	A	20000208	(200015)*		95

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6022544	A	Cont of	US 1983-460266	19830124
		Cont of	US 1986-869808	19860529
		CIP of	US 1988-248293	19880921
		CIP of	US 1989-354710	19890522
		CIP of	US 1990-628858	19901217
		Cont of	US 1991-808797	19911217
			US 1995-391267	19950221

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 6022544	A	CIP of	US 5126131

PRIORITY APPLN. INFO: US 1991-808797 19911217; US 1983-460266 19830124; US 1986-869808 19860529; US 1988-248293 19880921; US 1989-354710 19890522; US 1990-628858 19901217; US

1995-391267 19950221

AN 2000-170661 [15] WPIDS

CR 1999-008274 [01]

AB US 6022544 A UPAB: 20000323

NOVELTY - A method (I) of specifically suppressing undesired high level immune responses to T-cell **antigens** using non-immunogenic constructs free of high molecular weight immunostimulatory molecules which bind to B-cell membrane immunoglobulin receptors but fail to form an immunon, is new.

DETAILED DESCRIPTION - A method (I) of specifically suppressing an undesired high level immune response to a T-dependent **antigen**, comprising administering (to a mammal) a non-immunogenic purified construct comprising an antigenically recognizable group (derived from the **antigen**) conjugated to an acceptable **carrier** solution. The undesired high level immune response is the production of an antibody after repeated exposures of the mammal to the **antigen**. The purified construct is free of high molecular weight immunostimulatory molecules.

The immune system recognizes foreign **antigens** in the context of physically constrained arrays. In order to stimulate the immune system the arrays must exceed a specific size (or geometry) and have a minimum number of physically accessible groups which are identical in nature (minimum valence). Once these two parameters are met or exceeded, the immune system will respond by the production of antibodies (immunoglobulin M (IgM), IgG and/or lgE) by **antigen** specific B-cells and by the production of **T-cell** factors and/or activities (for example, **T-cells** 'help' with cytokines and **cytotoxicity**).

The method (I) is based on the finding that this system can be manipulated by introducing synthetically derived macromolecular arrays that are subthreshold in geometry and/or valence and which are designed to compete with naturally occurring arrays for the suppression of autoimmune and extrinsic allergic responses.

USE - (I) may be used for suppressing undesirable high level immune responses such as those associated with autoimmune diseases.

Dwg.0/55

L21 ANSWER 8 OF 21 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000-136656 [12] WPIDS

CROSS REFERENCE: 1998-387767 [33]

DOC. NO. NON-CPI: N2000-102226

DOC. NO. CPI: C2000-041816

TITLE: Mucosal administration of substance e.g. vaccine by contacting mucosal surface with substance in combination with optionally coated natural polymer core e.g. crosslinked polysaccharide .

DERWENT CLASS: B07 P34

INVENTOR(S): BETBEDER, D; DE MIGUEL, I; ETIENNE, A; KRAVTZOFF, R; MAJOR, M
PATENT ASSIGNEE(S): (BIOV-N) BIOVECTOR THERAPEUTICS SA
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6017513	A	20000125	(200012)*		27

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6017513	A	CIP of	US 1996-774920	19961227
			US 1997-987436	19971209

PRIORITY APPLN. INFO: US 1997-987436 19971209; US 1996-774920 19961227
AN 2000-136656 [12] WPIDS
CR 1998-387767 [33]
AB US 6017513 A UPAB: 20000308
NOVELTY - Mucosal administration of substances to mammals comprises contacting a mucosal surface with the substance in combination with Biovector core comprising natural polymer and/or its hydrolysate that is uncoated or partially or completely coated with no more than one layer comprising lipid compound covalently bonded to the core or an amphiphilic compound.

ACTIVITY - Drug delivery.

The delivery system is used for mucosal administration of substances to mammals (claimed) including **therapeutic** or **prophylactic** agents (radiopharmaceutical, analgesic, anesthetic, anorectic, anti-anemic, anti-asthmatic, anti-diabetic, antihistamine, anti-inflammatory, antibiotics, antimuscarinic, antineoplastic, antiviral, cardiovascular drug, CNS depressant, CNS stimulator, antidepressant, anti-epileptic, anxiolytic, hypnotic, sedative, anti-psychotic, beta blocker, hemostatic, hormone, vasodilator, vasoconstrictor, vitamin, vaccines against pathogens including bacteria, viruses, yeasts or fungi, specifically influenza virus (preferred), cytomegalovirus, **human** immunodeficiency **virus**, papilloma **virus**, respiratory syncytial virus, poliomyelitis virus, pox virus, measles virus, arbor virus, Coxsackie virus, herpes virus, hantavirus, **hepatitis** virus, Lyme disease virus, mumps virus or rotavirus, Neisseria, Aerobacter, Pseudomonas, Porphyromonas, Salmonella, Escherichia, Pasteurella, Shigella, Bacillus, Helibacter (sic), Corynebacterium, Clostridium, Mycobacterium, Yersinia, Staphylococcus, Bordetella,

Brucella, Vibrio or Streptococcus, Plasmodium, Schisostoma or Candida, diagnostic agents such as contrast or imaging agent e.g. that detect corneal irregularities or those labeled with detectable groups (radioactive, magnetic or fluorescent), small chemical molecules (organic, inorganic or organo-metallic molecules) or biological molecules (amino acid, oligopeptide, peptide, **protein**, glycoprotein, lipoprotein, proteoglycan, lipopolysaccharide, fatty acid, eicosanoid, lipid, triglyceride, **phospholipid**, glycolipid, nucleoside, nucleotide, nucleic acid, DNA molecule, RNA molecule, monosaccharide, oligosaccharide or polysaccharide) (claimed) as well as cytokines, growth factors, enzymes, **antigens** (including epitopes of **antigens** and haptens), antibodies, hormones, (natural and synthetic hormones and their derivatives), co-factors, receptors, enkephalins, endorphins, neurotransmitter s and nutrients such as insulin, interferon (alpha -, beta - or gamma -IFN), interleukins (IL-1 to IL-15), interleukin receptors (IL-1 receptor), calcitonin, erythropoeitin, thrombopoietin, epidermal growth factor and insulin-like growth factor-1. It can also be used to detect irregularities within the respiratory tract, digestive tract, auditory canal, urethra, rectum or any part of mammal with mucosal membrane and to deliver contrast agents for magnetic resonance imaging.

Influenza hemagglutinin (HA) was delivered by Biovectors to female mice, with 5 mu g HA applied intranasally in 20 or 50 mu l of phosphate-buffered saline solution or suspension, either alone or in Biovector formulation. One group of animals was subjected to light ether anesthesia, while the others were awake. Administration of 20 mu l on the outer nostrils of awake animals restricted the **antigen** to the upper respiratory tract. Volume of 50 mu l directly into the nostrils of anesthetized animals resulted in deposition of at least some **antigen** in the lower respiratory tract and lung as well as in the nasal cavity. Four different Biovectors were used: (Q) **positive** and (P) **negatively charged** light Biovectors either re-suspended - (1Q) and (1P) - or dispersed (2Q) and (2P). Influenza virus subunit **antigen** was either pre-loaded in the Biovectors or post-loaded (admixed immediately prior to administration). **Antigen** alone was used as control (3). Mice were sacrificed at day 28 and serum samples from the vena porta analyzed by direct enzyme-linked immunosorbent assay (ELISA). Serum immunoglobulin G titers (geometric mean) determined as reciprocal of sample dilution corresponding to absorbance at 492 nm of 0.2 above background were as follows in unanesthetized animals: (1Q) pre-loaded = 10, post-loaded = 20; (1P) pre-loaded = 400, post-loaded = 30; (2Q) pre- and post-loaded = 2,000; (2P) pre- and post-loaded = 200, and as follows in anesthetized animals: (1Q) = 30; (1P) = 30; (2Q) 4,000; (2P) = 60. Control was 100 for

unanesthetized animals and 200 in anesthetized animals.

MECHANISM OF ACTION - None given.

ADVANTAGE - The system is capable of delivering substances to animals (including humans) efficiently and avoiding disadvantages of the prior art. The **carrier** directs substances to the mucosa in a non-specific manner, is capable of being loaded with the substance immediately prior to administration, is of a size susceptible to microfiltration for sterilization avoiding need for preservatives and it is stable for up to 12 months, even one or more years. Biovectors have larger relative surfaces and volumes than larger microspheres or nanospheres and multiple substances can be delivered per Biovector.

Dwg.0/11

L21 ANSWER 9 OF 21 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000374292 EMBASE

TITLE: Evaluation of a liposome-supplemented intranasal influenza subunit vaccine in a murine model system: Induction of systemic and local mucosal immunity.

AUTHOR: De Haan A.; Van Scharrenburg G.J.M.; Masihi K.N.; Wilschut J.

CORPORATE SOURCE: J. Wilschut, Department of Medical Microbiology, Molecular Virology Section, University of Groningen, Ant. Deusinglaan 1, 9713 AV Groningen, Netherlands. j.c.wilschut@med.rug.nl

SOURCE: Journal of Liposome Research, (2000) 10/2-3 (159-177).
Refs: 48
ISSN: 0898-2104 CODEN: JLREE7

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
039 Pharmacy

LANGUAGE: English

SUMMARY LANGUAGE: English

AB This study reports on the mucosal immunoadjuvant activity of liposomes in an experimental influenza subunit vaccine administered intranasally (i.n.) to mice. Antibody responses induced by the i.n. liposomal vaccine were compared to those induced by an influenza **infection** or by subcutaneous (s.c.) injection of subunit **antigen** alone, theconventional route of human flu vaccination. **Negatively charged** liposomes, but not **positively charged** or zwitterionic liposomes, coadministered i.n. with influenza subunit **antigen**, significantly stimulated systemic IgG levels and local antibody responses in pulmonary secretions, relative to the responses upon i.n. administration of subunit **antigen**

alone. I.n. immunization with liposome-supplemented subunit **antigen** as well as s.c. immunization with subunit **antigen** alone or **infection** induced high levels of IgG antibodies in serum and pulmonary secretions, with a preferential induction of IgG1 upon immunization and IgG2a upon **infection**. Both i.n. immunization with liposome-supplemented **antigen** and **infection**, but not s.c. immunization with subunit **antigen** alone, induced local secretion of S-IgA. At the same time, both IgA- and IgG-secreting cells appeared in the lungs and lung-associated lymph nodes, suggestive of local antibody production. In conclusion, the liposomal **adjuvant** system, combined with a mucosal administration protocol, provides a promising strategy for induction of both systemic and local antibody responses against influenza virus.

L21 ANSWER 10 OF 21 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000484690 MEDLINE
DOCUMENT NUMBER: 20385105 PubMed ID: 10924786
TITLE: Influence of antigenic forms and **adjuvants** on protection against a lethal **infection** of Aujeszky's disease virus.
AUTHOR: Katayama S; Oda K; Ohgitani T
CORPORATE SOURCE: Division of Veterinary Microbiology, Kyoto Biken Laboratories, 24-16 Makishima-cho, Kyoto 611-0041, Uji, Japan.
SOURCE: VACCINE, (2000 Aug 15) 19 (1) 54-8.
Journal code: X60; 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ED Entered STN: 20001019
Last Updated on STN: 20001019
Entered Medline: 20001011

AB The influence of antigenic forms and **adjuvant** types on protection against a lethal **infection** of Aujeszky's disease virus (ADV) in mice was investigated. Antiviral IgG2a antibody response against particulate (inactivated ADV) and soluble **antigen** (ADV solubilized with deoxychorate-Na) in approximate order of extent was ISA70>QS-21>**positively charged** liposome>**negatively charged** liposome>weak **negatively charged** liposome>ISA25>lablabside F **saponin**>aluminum phosphate gel>non **adjuvant**. Particulate **antigen** induced higher IgG2a antibody production than soluble **antigen**. Particulate **antigen** combined with ISA70, ISA25 or **positively charged** liposome gave 100, 50 and 40%

protection to mice, respectively. In contrast, soluble **antigen** plus ISA70 conferred 30% protection on mice. Immunogens using the other **adjuvants** gave </=20% protection to mice. These results indicate that a combination of particulate **antigen** and an appropriate **adjuvant** effectively induces the production of antiviral IgG2a antibody and provides protection against a lethal ADV **infection** in mice.

L21 ANSWER 11 OF 21 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-357731 [30] WPIDS
DOC. NO. CPI: C1999-105839
TITLE: Use of **phospholipids** as antimicrobial agents.
DERWENT CLASS: B05 C01 C03 D21 D22
INVENTOR(S): COHEN, P S; KROGFELT, K A; LAUX, D C; UTLEY, M
PATENT ASSIGNEE(S): (STAT-N) STATENS SERUMINSTITUT; (STAT-N) STATENS SERUM INST
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9926632	A1	19990603	(199930)*	EN	43
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9913337	A	19990615	(199944)		
EP 1051180	A1	20001115	(200059)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 6165997	A	20001226	(200103)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9926632	A1		WO 1998-DK512	19981120
AU 9913337	A		AU 1999-13337	19981120
EP 1051180	A1		EP 1998-956826	19981120
			WO 1998-DK512	19981120
US 6165997	A	Provisional	US 1997-66901	19971120
			US 1998-196354	19981119

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9913337	A	Based on	WO 9926632
EP 1051180	A1	Based on	WO 9926632

PRIORITY APPLN. INFO: US 1997-66901 19971120; US 1998-196354 19981119

AN 1999-357731 [30] WPIDS

AB WO 9926632 A UPAB: 19990802

NOVELTY - Use of **phospholipids** (I) as antimicrobials or as enhancers of antimicrobials is new.

DETAILED DESCRIPTION - Use of **phospholipids** of formula (I) as medicament is new.

Z = P or S oxyacid residue;

R1, R2 = OH or an optionally saturated fatty acid residue with at least 7C;

provided that only one of R1 and R2 = OH; and

R3 = H or an uncharged, **negatively charged**, or **positively charged** group derived from an OH-containing compound by removal of the hydroxy group.

INDEPENDENT CLAIMS are also included for:

(1) the use of (I) in which R3 is H or a group derived from a OH-containing compound with an overall **negative** or neutral **charge** such as inositol, glycerol, ethanolamine, especially serine, for the manufacture of a medicament for the **treatment** of an animal with an infectious disease, especially caused by a Gram **negative** bacterium; and

(2) the use of (I) in combination with an antimicrobial as a medicament with synergistic antimicrobial effect.

ACTIVITY - Antibacterial; antifungal; antiviral; antiprotozoal.

MECHANISM OF ACTION - Enhance antimicrobial activity by taking Ca and Mg form the lipopolysaccharide (LPS) of the outer membrane causing a release of LPS. This destabilizes the membrane and permeabilizes it to the antimicrobial.

USE - As antimicrobial agents for **prophylaxis** or **treatment** of **infections** caused by Gram **negative** and Gram **positive** bacterium. (I) may be formulated as a paste and used for **treating** wound burns, ulcus cruris and acne; as a liquid for **treating** eye **infection**, periodontitis, otitis, mouth- and throat **infections**; or as a vapor for **treating** lung **infections**. (I) may be used in humans and in animals, especially in farm animals and particularly for **prophylaxis** of a disease caused by primary **infection**. (I) may also be used in cosmetics, for disinfection, personal hygiene or as preservatives, for protection of plants against bacterial **infection** or for combating bacterial **infections** on plants (all claimed). Plant pathogens which can be combated using

(I) include Pseudomonas, Xanthomonas, erwinia, Corynebacterium, Streptomyces, Mycoplasma or Spirioplasma in e.g. tobacco, beans, peas, soybeans, lilac, banana, sugar cane, corn, potato, tomato and raspberries. (I) are particularly useful for disinfecting surfaces, household utilities, industrial utilities or contact lenses; athletes's foot, sore throat, bad breath, or hand lotion for dry skin with small rashes; for disinfecting dental utilities, dental implant and dental protheses; in shampoos, candies, ointments, tooth paste or foam sprays; for preservation and/or disinfection of food. (I) may be used in pets e.g. cats, dogs or guinea pigs or zoo animals. The farm animals may be cattle, horse, pig mink, goat, sheep or a bird such as chicken, ostrich, turkey, duck or goose. (I) may also be used to enhance the effect of other antimicrobials, preferably those which act through inhibition of cell wall synthesis such as beta -lactams and vancomycin, especially penicillins (e.g. penicillin G and V), cephalosporins (e.g. cefadroxil and ceftizoxime), carbapenems (e.g. imipenem) or monobactams. (I) may also be used to enhance the action of tetracycline antibiotics (especially to decrease tetracycline resistance), antimicrobials acting through inhibition of **protein** synthesis e.g. chloramphenicol, or through inhibition of nucleic acid synthesis e.g. sulfonamides such as sulfacytine. (I) may be used **treat** protozoa such as Entamoeba histolytica or Plasmodium. Oral formulations of (I) may be used to **treat** gastritis, typhus, gastroenteritis, anthrax, botulim, pseudomembranous colitis, dysentry, enterocolitis, peritonitis, abscess, pertussis, cholera, pestis, cystitis, pneumonia, meningitis and Crohn's disease; lung **infections** include cystic fibrosis, diphtheria, pertussis (whooping cough), epiglottitis, nasopharyngitis, bronchitis and tonsilitis; others include gonorrhoea (including urethritis, endocervicitis and proctitis), tetanus, gas gangrene scarlatina, erysipelas, sycosis barbae, folliculitis, impetigo contagiosa or impetigo bullosa. Eye **infection** include orbital and cellulitis, conjunctivitis.

ADVANTAGE - (I) are non-toxic since **phospholipids** are natural substances. Use of (I) avoids or decreases the emergence of antibiotic resistant strains of bacteria.

Dwg.0/0

L21 ANSWER 12 OF 21 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 1999401153 MEDLINE

DOCUMENT NUMBER: 99401153 PubMed ID: 10469918

TITLE: **Positively charged** liposome functions as an efficient immunoadjuvant in inducing cell-mediated immune response to soluble **proteins**.

AUTHOR: Nakanishi T; Kunisawa J; Hayashi A; Tsutsumi Y; Kubo K; Nakagawa S; Nakanishi M; Tanaka K; Mayumi T

CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Osaka University, 1-6, Yamadaoka, Suita, Osaka, Japan.
SOURCE: JOURNAL OF CONTROLLED RELEASE, (1999 Aug 27) 61 (1-2) 233-40.
Journal code: C46; 8607908. ISSN: 0168-3659.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ED Entered STN: 19991026
Last Updated on STN: 19991026
Entered Medline: 19991013

AB In order to design an optimized liposome immunoadjuvant for inducing cell-mediated immune response against soluble proteinaceous **antigens**, we investigated the effect of liposomal surface **charge** on the immunoadjuvant action. **Positively charged** liposomes containing soluble **antigens** functioned as a more potent inducer of **antigen**-specific **cytotoxic T lymphocyte** responses and delayed type hypersensitivity response than **negatively charged** and neutral liposomes containing the same concentrations of **antigens**. To clarify the reason of the differential immune response, we examined the delivery of soluble **proteins** by the liposomes into the cytoplasm of macrophages, using fragment A of diphtheria toxin (DTA) as a marker. We found that **positively charged** liposomes encapsulating DTA are **cytotoxic** to macrophages, while empty **positively charged** liposomes, DTA in **negatively charged** and neutral liposomes are not. Consistent with this, only macrophages pulsed with OVA in **positively charged** liposomes could significantly stimulate OVA-specific, class I MHC-restricted **T cell** hybridoma. These results suggest that the **positively charged** liposomes can deliver proteinaceous **antigens** efficiently into the cytoplasm of the macrophages/**antigen**-presenting cells, where the **antigens** are processed to be presented by class I MHC molecules to induce the cell-mediated immune response. Possible development of the safe and effective vaccine is discussed.

L21 ANSWER 13 OF 21 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3
ACCESSION NUMBER: 1998:394662 BIOSIS
DOCUMENT NUMBER: PREV199800394662
TITLE: Cationization of liposomal surface **charge** enhances **adjuvant** effect of liposomes for tumor vaccine.
AUTHOR(S): Nakanishi, Tsuyoshi; Kunisawa, Jun; Hayashi, Akira;

Tsutsumi, Yasuo; Hayakawa, Takao; Mayumi, Tadanori (1)
CORPORATE SOURCE: (1) Graduate Sch. Pharmaceutical Science, Osaka Univ., 1-6 Yamadaoka, Suita, Osaka 565-0871 Japan
SOURCE: Yakuzaigaku, (June, 1998) Vol. 58, No. 2, pp. 59-68. ISSN: 0372-7629.
DOCUMENT TYPE: Article
LANGUAGE: Japanese
SUMMARY LANGUAGE: English
AB In order to design an optimum liposome immunoadjuvant for tumor vaccines, we investigated the relationship between liposomal surface **charge** and **adjuvant** action. **Positively charged** multilamellar vesicles (MLVs) were taken up efficiently by macrophages, while **negatively charged** and neutral MLVs were hardly picked up. Consistent with this, **positively charged** MLVs containing soluble ovalbumin (OVA) functioned as a more potent inducer of **antigen**-specific **cytotoxic T lymphocyte** (CTL) responses and antibody production than **negatively charged** and neutral MLVs containing the same concentrations of **antigens**. Furthermore, the in vivo anti-tumor effects of variously **charged** liposomal **antigens** were examined using a Meth A tumor model and a crude butanol extract derived from Meth A (Meth A-CBE) as the tumor-associated **antigen**. Mice vaccinated with **positively charged** MLVs containing Meth A-CBE showed significant inhibition of Meth A tumor growth compared to mice vaccinated with Meth A-CBE alone or mice vaccinated with neutral or **negatively charged** liposomal Meth A-CBE. The injection of carrageenan into mice led to a significant loss of anti-tumor vaccinal effect of **positively charged** liposomal Meth A-CBE, which may be due to the inhibition of uptake and **antigen** presentation of liposomal **antigens** by macrophages as a result of a lack of macrophages in the immune site. Our results indicate that the **positive charge** on the surface of liposomes represents an important factor for enhancing their immunoadjuvancy in the induction of **antigen**-specific immune responses and vaccinal effects against tumors.

L21 ANSWER 14 OF 21 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1998063319 MEDLINE
DOCUMENT NUMBER: 98063319 PubMed ID: 9398647
TITLE: **Positively charged** liposome functions as an efficient immunoadjuvant in inducing immune responses to soluble **proteins**.
AUTHOR: Nakanishi T; Kunisawa J; Hayashi A; Tsutsumi Y; Kubo K; Nakagawa S; Fujiwara H; Hamaoka T; Mayumi T

CORPORATE SOURCE: Faculty and Graduate School of Pharmaceutical Science, Osaka University, Japan.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1997 Nov 26) 240 (3) 793-7.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ED Entered STN: 19980129
Last Updated on STN: 19980129
Entered Medline: 19980113

AB To design an optimum liposome immunoadjuvant for soluble **protein antigens**, we investigated the relationship between liposomal surface **charge** and **adjuvant** action. **Positively charged** multilamellar vesicles (MLV) were taken up efficiently by macrophages, while **negatively charged** and neutral MLVs were hardly picked up. Consistent with this, **positively charged** MLVs containing soluble chicken egg albumin (OVA) functioned as a more potent inducer of **antigen**-specific **cytotoxic T lymphocyte** (CTL) responses and antibody production than **negatively charged** and neutral MLVs containing the same concentrations of **antigens**. These results indicate that the **positive charge** on the surface of liposomes represents an important factor for enhancing their immunoadjuvancy in the induction of **antigen**-specific immune responses.

L21 ANSWER 15 OF 21 JICST-EPlus COPYRIGHT 2001 JST
ACCESSION NUMBER: 970378934 JICST-EPlus
TITLE: Particle design of liposome as tumor vaccine **adjuvant**. Increasing effect of the liposome **adjuvant** by cationization.
AUTHOR: NAKANISHI TSUYOSHI; KUNISAWA JUN; HAYASHI TETSU; NAKAGAWA SHINSAKU; MAYUMI TADANORI FUJIWARA HIROMI; HAMAOKA TOSHIYUKI
CORPORATE SOURCE: Osaka Univ., Fac. of Pharm. Sci.
Osaka Univ., Biomed. Res. Center
SOURCE: Yakuzaigaku (Journal of Pharmaceutical Science and Technology, Japan), (1997) vol. 57, no. Suppl, pp. 114-115. Journal Code: G0234A (Fig. 3, Ref. 3)
CODEN: YAKUA2; ISSN: 0372-7629
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Short Communication
LANGUAGE: Japanese
STATUS: New

AB The above-mentioned cationization was examined in order to promote the uptake to macrophage (M).The adsorption to M was slight for liposome (L) of **negative charge** and neuteral **charge**, and there was seldom an uptake.In the meantime, the uptake increased at 37.DEG.C. in the case of L of **positive charge**.**Antigen** specific **cytotoxic T cells** were induced in the case of a **positive charge** L administered group.These results showed that **positive** electric **charge** L promoted **antigen** processing and **antigen** presentation of M and that it induced the **cytotoxic T c lls**.

L21 ANSWER 16 OF 21 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1996-171394 [17] WPIDS
DOC. NO. CPI: C1996-054049
TITLE: Inducing protection against **infection** -associated abscess formation - by admin. of Bacteroides fragilis polysaccharide A or related polymer.
DERWENT CLASS: B04
INVENTOR(S): KASPER, D L; ONDERDONK, A B; TZIANABOS, A O; KASPER, O
PATENT ASSIGNEE(S): (BGHM) BRIGHAM & WOMENS HOSPITAL
COUNTRY COUNT: 66
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9607427	A1	19960314	(199617)*	EN	40
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG					
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG UZ VN					
AU 9535439	A	19960327	(199627)		
EP 778780	A1	19970618	(199729)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
US 5679654	A	19971021	(199748)		17
US 5700787	A	19971223	(199806)		17
JP 10507746	W	19980728	(199840)		42
AU 702325	B	19990218	(199919)		
AU 9913217	A	19990318	(199923)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 9607427	A1		WO 1995-US11160	19950901
AU 9535439	A		AU 1995-35439	19950901
EP 778780	A1		EP 1995-932380	19950901
			WO 1995-US11160	19950901
US 5679654	A		US 1994-301271	19940902
US 5700787	A	CIP of	US 1994-301271	19940902
			US 1995-502865	19950714
JP 10507746	W		WO 1995-US11160	19950901
			JP 1996-509606	19950901
AU 702325	B		AU 1995-35439	19950901
AU 9913217	A	Div ex	AU 1995-35439	19950901
			AU 1999-13217	19990127

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9535439	A	Based on	WO 9607427
EP 778780	A1	Based on	WO 9607427
JP 10507746	W	Based on	WO 9607427
AU 702325	B	Previous Publ.	AU 9535439
		Based on	WO 9607427
AU 9913217	A	Div ex	AU 702325

PRIORITY APPLN. INFO: US 1995-502865 19950714; US 1994-301271 19940902

AN 1996-171394 [17] WPIDS

AB WO 9607427 A UPAB: 19960428

(A) Inducing protection against abscess formation associated with **infection** comprises admin. of a polymer comprising repeating units with the same **charge** pattern as Bacteroides fragilis polysaccharide A (PSA), i.e. a **positively charged** amino gp. and a **negatively charged** carboxyl, phosphate, phosphonate, sulphate or sulphonate gp., provided that the polymer is not in the form of B. fragilis capsular polysaccharide complex. Also claimed are: (B) a pharmaceutical prepn. for the above purpose, contg. a polymer as above with at most 10 repeating units, other than S. pneumoniae polysaccharide, T. cruzi lipopeptidophosphoglycan and P. aeruginosa Fisher immunotype 7 O-**antigen**; and (C) a process for preparing a pharmaceutical compsn. for the above purpose comprising: (a) preparing a polymer as above from a corresp. precursor polymer by converting a precursor gp. into a **positively charged** amino gp.; and (b) combining the polymer with a **carrier**.

USE - The method is esp. useful for **prophylaxis** of abdominal abscess formation associated with leakage of colonic bacteria into the peritoneal cavity, e.g. during surgery, trauma or

diseases such as appendicitis or cancer. The polymer is administered parenterally in doses of 1 ng/kg to 100 mg/kg, pref. 1-100 mug/kg.
Dwg.0/0

ABEQ US 5679654 A UPAB: 19971209
A method for inducing protection against abscess formation associated with **infection** comprising:

administering to a subject in need of such protection a pharmaceutical preparation containing an effective amount, for inducing protection against abscess formation, of a polysaccharide formed of repeating units with each repeating unit being formed of a maximum of ten monosaccharides, wherein each repeating unit includes a free amino moiety and a **negatively charged** moiety selected from the group consisting of carboxyl, phosphate and phosphonate, and wherein the polysaccharide is free from dimerisation as part of a B. fragilis capsular polysaccharide complex.
Dwg.0/0

ABEQ US 5700787 A UPAB: 19980209
(A) Inducing protection against abscess formation associated with **infection** comprises admin. of a polymer comprising repeating units with the same **charge** pattern as Bacteroides fragilis polysaccharide A (PSA), i.e. a **positively charged** amino gp. and a **negatively charged** carboxyl, phosphate, phosphonate, sulphate or sulphonate gp., provided that the polymer is not in the form of B. fragilis capsular polysaccharide complex. Also claimed are: (B) a pharmaceutical prepn. for the above purpose, contg. a polymer as above with at most 10 repeating units, other than S. pneumoniae polysaccharide, T. cruzi lipopeptidophosphoglycan and P. aeruginosa Fisher immunotype 7 O-**antigen**; and (C) a process for preparing a pharmaceutical compsn. for the above purpose comprising: (a) preparing a polymer as above from a corresp. precursor polymer by converting a precursor gp. into a **positively charged** amino gp.; and (b) combining the polymer with a **carrier**.

USE - The method is esp. useful for **prophylaxis** of abdominal abscess formation associated with leakage of colonic bacteria into the peritoneal cavity, e.g. during surgery, trauma or diseases such as appendicitis or cancer. The polymer is administered parenterally in doses of 1 ng/kg to 100 mg/kg, pref. 1-100 mu g/kg.
Dwg.0/0

L21 ANSWER 17 OF 21 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1995-263655 [34] WPIDS
DOC. NO. CPI: C1995-120063
TITLE: Compsn. contg. nucleic acid and lipo-poly amine - at specific **charge** ratio, provides efficient transfer of nucleic acid to cells or

organs, e.g. for in vivo prodn. of **therapeutic protein.**

DERWENT CLASS: B04 D16

INVENTOR(S): BEHR, J; DEMENEIX, B; REMY, J; SCHERMAN, D; SCHWARTZ, B; SCHERMANN, D

PATENT ASSIGNEE(S): (RHON) RHONE-POULENC RORER SA; (RHON) RHONE POULENC RORER SA; (CNRS) CENT NAT RECH SCI; (AVET) AVENTIS PHARMA SA

COUNTRY COUNT: 61

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9518863	A1	19950713	(199534)*	FR	24
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ					
W: AM AU BB BG BR BY CA CN CZ EE FI GE HU JP KE KG KP KR KZ LR LT LV MD MG MN MW MX NO NZ PL RO RU SD SI SK TJ TT UA US UZ VN					
FR 2714830	A1	19950713	(199534)		
AU 9514583	A	19950801	(199546)		
ZA 9500137	A	19951129	(199601)		31
NO 9602791	A	19960702	(199639)		
FI 9602799	A	19960709	(199641)		
EP 738328	A1	19961023	(199647)	FR	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
JP 09508100	W	19970819	(199743)		25
KR 97700248	A	19970108	(199801)		
MX 9602561	A1	19970301	(199820)		
US 5846947	A	19981208	(199905)		
AU 707571	B	19990715	(199939)		
US 6172048	B1	20010109	(200104)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9518863	A1	WO 1995-FR22	19950109
FR 2714830	A1	FR 1994-159	19940110
AU 9514583	A	AU 1995-14583	19950109
ZA 9500137	A	ZA 1995-137	19950110
NO 9602791	A	WO 1995-FR22	19950109
		NO 1996-2791	19960702
FI 9602799	A	WO 1995-FR22	19950109
		FI 1996-2799	19960709
EP 738328	A1	EP 1995-906377	19950109
		WO 1995-FR22	19950109
JP 09508100	W	JP 1995-518346	19950109

			WO 1995-FR22	19950109
KR 97700248	A		WO 1995-FR22	19950109
			KR 1996-703770	19960712
MX 9602561	A1		MX 1996-2561	19960701
US 5846947	A		WO 1995-FR22	19950109
			US 1996-666308	19960710
AU 707571	B		AU 1995-14583	19950109
US 6172048	B1	Cont of	WO 1995-FR22	19950109
		Cont of	US 1996-666308	19960710
			US 1998-160937	19980925

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9514583	A	Based on	WO 9518863
EP 738328	A1	Based on	WO 9518863
JP 09508100	W	Based on	WO 9518863
KR 97700248	A	Based on	WO 9518863
US 5846947	A	Based on	WO 9518863
AU 707571	B	Previous Publ.	AU 9514583
		Based on	WO 9518863
US 6172048	B1	Cont of	US 5846947

PRIORITY APPLN. INFO: FR 1994-159 19940110
AN 1995-263655 [34] WPIDS
AB WO 9518863 A UPAB: 20010207
Pharmaceutical compsn. comprises a nucleic acid (I) and a lipopolyamine (II) with ratio (R) between **positive charges** on (II) and **negative charges** on (I) at most 2. Also claimed is compsn. of (I), (II) and an **adjuvant** (III) that can associate with the (I)-(II) complex so as to increase its transfecting capacity.

USE - The compsn. can be used for (I) (gene) transfer, e.g. for expressing a **protein** that is deficient or defective (e.g. an enzyme, hormone, factor VIII); for blocking expression of a partic. gene or to generate an **antigen** in vivo for immunotherapy of viral **infection** or cancer.

ADVANTAGE - The compsns. provide very effective in vivo transfer of (I) into cells and/or organs without toxicity. Large amounts of (I) can be delivered and the compsns. avoid difficulties associated with use of viral vectors.

Dwg.0/0

L21 ANSWER 18 OF 21 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95235153 EMBASE
DOCUMENT NUMBER: 1995235153
TITLE: Protective effect of Brucella outer membrane

complex-bearing liposomes against experimental murine brucellosis.
AUTHOR: Vitas A.I.; Diaz R.; Gamazo C.
CORPORATE SOURCE: Departamento de Microbiologia, Universidad de Navarra,31080 Pamplona, Spain
SOURCE: FEMS Microbiology Letters, (1995) 130/2-3 (231-236). ISSN: 0378-1097 CODEN: FMLED7
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Liposomes of stable multilamellar type, which previously demonstrated great efficiency in antibiotic transport, were used in this study as transport vehicles of antigenic extracts of Brucella melitensis (HS: complex of lipopolysaccharide/**phospholipids** /outer membrane **proteins**). The incorporation of HS into **positively charged** liposomes produced a protective effect against experimental murine brucellosis when they were administered 1 day before or 2 days after **infection**, as the number of colony-forming units in the spleen was reduced in relation to the untreated control group ($P < 0.01$). On the other hand, the use of HS-free or bound in liposomes with **negative** net **charge** did not produce a significant effect. Moreover, the incorporation of HS into cationic liposomes eliminated the toxicity of the lipopolysaccharide.

L21 ANSWER 19 OF 21 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 94346664 MEDLINE
DOCUMENT NUMBER: 94346664 PubMed ID: 8067610
TITLE: Adjuvanted subunit vaccines for the control of Salmonella enteritidis **infection** in turkeys.
AUTHOR: Charles S D; Hussain I; Choi C U; Nagaraja K V; Sivanandan V
CORPORATE SOURCE: Department of Veterinary PathoBiology, College of Veterinary Medicine, University of Minnesota, St Paul 55108.
SOURCE: AMERICAN JOURNAL OF VETERINARY RESEARCH, (1994 May) 55 (5) 636-42.
Journal code: 40C; 0375011. ISSN: 0002-9645.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409

Searcher : Shears 308-4994

ED Entered STN: 19941005
Last Updated on STN: 19941005
Entered Medline: 19940916

AB Liposomes and immunostimulating complexes (ISCOM) are **adjuvants** that have been known to potentiate the immune response to membrane **proteins**. Adjuvanted outer membrane **proteins** (OMP) from Salmonella enteritidis were evaluated for their protective efficacy against S enteritidis **infection** in turkeys. The adjuvanted vaccines prepared for evaluation were: **positive** or **negatively charged** liposomes, lipid-conjugated ISCOM, and mineral oil vaccines. These preparations were compared with that of a whole cell bacterin and **protein** alone. After vaccination, turkeys were challenge-exposed with a nalidixic acid-resistant strain of S enteritidis. They were monitored for clinical signs of disease, antibody response, bacterial shedding pattern, and clearance of the challenge S enteritidis from internal organs. Results indicated a significantly ($P < 0.05$) higher antibody response to the **positively charged** liposomal OMP vaccine, compared with the whole cell bacterin. The antibody response to **positively charged** liposomal OMP vaccine was greater when a booster dose of this preparation was given. Shedding of S enteritidis was decreased in all vaccinated and challenge-exposed turkeys ($P < 0.001$). The tissues from a high percentage (90 to 100%) of birds that received a booster vaccination of the liposomal (+ or -) and ISCOM vaccine were culture-**negative** for S enteritidis.

L21 ANSWER 20 OF 21 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 92224597 MEDLINE
DOCUMENT NUMBER: 92224597 PubMed ID: 1563240
TITLE: Antiphospholipid antibody syndrome.
AUTHOR: Sammaritano L R; Gharavi A E
CORPORATE SOURCE: Division of Rheumatic Diseases, Hospital for Special Surgery, Cornell University Medical Center, New York, New York.
SOURCE: CLINICS IN LABORATORY MEDICINE, (1992 Mar) 12 (1) 41-59. Ref: 162
Journal code: DLS; 8100174. ISSN: 0272-2712.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ED Entered STN: 19920607
Last Updated on STN: 19920607

Entered Medline: 19920521

AB Autoimmune aPL are associated with a well-defined clinical syndrome of vascular thromboses, recurrent fetal loss, thrombocytopenia, livedo reticularis, and valvular and neurologic abnormalities. A clinical diagnosis of SLE need not be present, and aPL syndrome in the absence of other well-defined autoimmune disease is termed PAPS. A **positive** test for aPL is defined by enzyme-linked immunoassay (aCL) or by functional coagulation assay (LAC). Anticardiolipin antibody and LAC are similar but probably not identical antibodies. The false-**positive** test for syphilis is less closely associated with clinical complications than are aCL and LAC. The mechanism of action of aPL is not yet known, although many theories have been advanced. Recent identification of beta 2-glycoprotein I, a serum glycoprotein, as an aPL cofactor suggests that inhibition of this **protein**'s anticoagulant activity may be important. Autoimmune aPL differ from **infection** -induced aPL in important antibody characteristics, including IgG subclass, light chain preference, antibody avidity, and cofactor requirement. Both recognize **negatively charged** **phospholipids**, but various physical characteristics of the **phospholipids** alter the recognition patterns. **Treatment** of the aPL syndrome is not well defined. Anticoagulation with heparin, coumadin, or aspirin are currently widely used. Although corticosteroid, immunosuppressive **therapy**, and plasmapheresis may be used for severe, fulminant thrombosis, the efficacy of this **treatment** has yet to be proved.

L21 ANSWER 21 OF 21 MEDLINE

ACCESSION NUMBER:	91331588 MEDLINE
DOCUMENT NUMBER:	91331588 PubMed ID: 1869286
TITLE:	Serum factors affecting the specificity of anticardiolipin antibodies.
AUTHOR:	Layton G T; Johnston S C; Bertwistle N G
CORPORATE SOURCE:	Research and Development Laboratories, Medical Innovations Ltd, Labrador, Qld, Australia.
SOURCE:	IMMUNOLOGY AND CELL BIOLOGY, (1991 Feb) 69 (Pt 1) 17-25. Journal code: GH8; 8706300. ISSN: 0818-9641.
PUB. COUNTRY:	Australia
	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	199109
ED	Entered STN: 19911006
	Last Updated on STN: 19911006
	Entered Medline: 19910918

AB The effects were investigated of two pretreatments of human serum

and plasma test samples on their subsequent reactivity in the anticardiolipin antibody enzyme-linked immunosorbent assay (ACA-ELISA). The first **treatment** involved heat inactivation of test samples at 56 degrees C for 30 min, a process sometimes used to inactivate samples from suspected **human** immunodeficiency **virus positive** individuals. Such **treatment** significantly increased the IgG ACA unit/mL values of normal sera, but when this effect was examined further, it was found that the increase in binding occurred on both **cardiolipin**-coated and uncoated wells and was therefore non-specific. Heat inactivation of sera prior to ACA testing should therefore be avoided. The second **treatment** involved diluting immunoglobulin (Ig)G and IgM ACA-**positive** sera in normal human serum (NHS) or newborn calf serum (NCS); sera diluted in NHS showed a significant increase in titre, particularly IgM ACA-**positive** sera. This phenomenon was found to be due to a serum **cardiolipin**-binding cofactor which enhances antibody recognition. The cofactor is heat stable and is present in normal sera (male and female) and also in IgG ACA-**positive** sera. The binding of a human IgM monoclonal antibody to **cardiolipin** was not affected by the cofactor. The **cardiolipin**/cofactor complex may represent the optimal autoantigen/autoimmunogen and a re-appraisal, therefore, of the clinical relevance of antibodies to **cardiolipin** and other **negatively charged** molecules is warranted.

FILE 'CAPLUS' ENTERED AT 14:45:18 ON 24 APR 2001

L1	(1)	SEA FILE=REGISTRY ABB=ON PLU=ON	SAPONIN/CN
L2	(1)	SEA FILE=REGISTRY ABB=ON PLU=ON	PHOSPHOLIPIDS/CN
L3	(1)	SEA FILE=REGISTRY ABB=ON PLU=ON	PHOSPHOGLYCERIDES/CN
L4	(2)	SEA FILE=REGISTRY ABB=ON PLU=ON	"MONOPHOSPHORYL LIPID A"/CN
L5	(1)	SEA FILE=REGISTRY ABB=ON PLU=ON	"OM 174"/CN
L6	(6)	SEA FILE=REGISTRY ABB=ON PLU=ON	L1 OR L2 OR L3 OR L4 OR L5
L7	(1)	SEA FILE=REGISTRY ABB=ON PLU=ON	"PHOSPHATIDIC ACIDS"/CN
L8	7	SEA FILE=REGISTRY ABB=ON PLU=ON	L6 OR L7
L9	406206	SEA FILE=CAPLUS ABB=ON PLU=ON	L8 OR CARRIER OR ADJUVANT OR SAPONIN OR ISCOMATRIX OR PHOSPHOLIPID OR PHOSPHOGLYCERIDE OR PHOSPHO(W)(LIPID OR GLYCERIDE) OR PHOSPHATIDYL(W)(INOSITOL OR GLYCERIDE) OR PHOSPHATIDYLINOSITOL OR PHOSPHATIDYLGLYCERIDE OR PHOSPHATIDIC OR CARDIOLIPIN OR LIPID(W)A OR CARDIO LIPIN OR OM174 OR OM 174
L10	75472	SEA FILE=CAPLUS ABB=ON PLU=ON	L9 AND (ANTIGEN OR PROTEIN)
L11	2584	SEA FILE=CAPLUS ABB=ON PLU=ON	L10 AND CHARG?

Searcher : Shears 308-4994

L12 619 SEA FILE=CAPLUS ABB=ON PLU=ON L11 AND POSITIV?
L13 337 SEA FILE=CAPLUS ABB=ON PLU=ON L12 AND NEGATIV?
L22 7 SEA FILE=CAPLUS ABB=ON PLU=ON L13 AND (CANCER? OR CARCIN? OR NEOPLAS? OR TUMOR OR TUMOUR)

=> s l22 not l14
L23 5 L22 NOT L14

L23 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:583942 CAPLUS
DOCUMENT NUMBER: 133:277402
TITLE: A potential mechanism for fumonisin B1-mediated hepatocarcinogenesis: cyclin D1 stabilization associated with activation of Akt and inhibition of GSK-3.beta. activity
AUTHOR(S): Ramljak, Danica; Calvert, Richard J.; Wiesenfeld, Paddy W.; Diwan, Bhalchandra A.; Catipovic, Branimir; Marasas, Walter F. O.; Victor, Tommie C.; Anderson, Lucy M.; Gelderblom, Wentzel C. A.
CORPORATE SOURCE: Laboratory of Comparative Carcinogenesis, Frederick Cancer Research and Development Center, National Cancer Institute, Frederick, MD, 21702, USA
SOURCE: Carcinogenesis (2000), 21(8), 1537-1546
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fumonisin B1 (FB1) is a worldwide corn contaminant and has been epidemiol. linked to the high incidence of human esophageal **cancer** in South Africa and China. FB1 is hepatocarcinogenic in rats by an unknown mechanism. Inhibition of ceramide synthase and disruption of membrane **phospholipids** have been shown to be mechanisms of toxicity. Here we show over-expression of cyclin D1 **protein** in both preneoplastic and **neoplastic** liver specimens obtained from a long-term feeding study of FB1 in rats. In rats fed FB1 short-term, cyclin D1 **protein** levels in liver were increased up to five-fold in a dose-responsive manner. Northern blot anal. demonstrated no increase in mRNA levels of cyclin D1. The 2D electrophoresis of cyclin D1 **protein** in FB1-treated samples showed a distinct pattern of migration (presence of less **neg.** **charged** form of the **protein**) that differed from controls. Recently, it has been shown that phosphorylation of cyclin D1 by glycogen synthase kinase 3.beta. (GSK-3.beta.) on a single threonine residue (Thr-286) **pos.** regulates proteosomal degrdn. of cyclin D1. In FB1-treated samples we

detected GSK-3.beta. phosphorylated on serine 9; activated **protein** kinase B (Akt) appears to be responsible for this activity-inhibiting phosphorylation. These findings suggest that over-expression of cyclin D1 results from stabilization due to a lack of phosphorylation mediated by GSK-3.beta.. We also obsd. an increase in cyclin dependent kinase 4 (Cdk4) complexes with cyclin D1 in FB1-treated samples; addnl., elevated Cdk4 activity was shown by increased phosphorylation of the retinoblastoma **protein** . In summary, the activation of Akt leads to increased survival, inhibition of GSK-3.beta. activity and post-translational stabilization of cyclin D1, all events responsible for disruption of the cell cycle G1/S restriction point in hepatocytes. This is the first report suggesting the mechanism by which FB1 acts as a **carcinogen**.

REFERENCE COUNT: 60

REFERENCE(S):
(1) Alessi, D; EMBO J 1996, V15, P6541 CAPLUS
(2) Bartek, J; Curr Opin Cell Biol 1996, V8, P805 CAPLUS
(3) Bartkova, J; Oncogene 1998, V17, P1027 CAPLUS
(4) Bianchi, A; Oncogene 1993, V8, P1127 CAPLUS
(5) Cantley, L; Proc Natl Acad Sci USA 1999, V96, P4240 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:708880 CAPLUS

DOCUMENT NUMBER: 131:319884

TITLE: Targetable encapsulated gas microbubbles for separation of target material from liquid samples and separation apparatus

INVENTOR(S): Cuthbertson, Alan; Rongved, Pal; Lovhaug, Dagfinn; Fjerdingstad, Hege; Solbakken, Magne; Godal, Aslak

PATENT ASSIGNEE(S): Nycomed Imaging As, Norway

SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955837	A2	19991104	WO 1999-GB1317	19990428
WO 9955837	A3	20000210		

W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE,

GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9937197	A1	19991116	AU 1999-37197	19990428
EP 1073716	A2	20010207	EP 1999-919396	19990428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NO 2000005383	A	20001213	NO 2000-5383	20001026

PRIORITY APPLN. INFO.:

GB 1998-9083	A	19980428
GB 1998-9085	A	19980428
US 1998-85819	P	19980518
US 1998-85826	P	19980518
WO 1999-GB1317	W	19990428

AB Sepn. of target material from a liq. sample is achieved by coupling the target to targetable encapsulated gas microbubbles, allowing the microbubbles and coupled target to float to the surface of the sample to form a floating microbubble/target layer, and sepg. this layer from the sample. In a **pos**. sepn. process the microbubbles are then removed from the target, e.g. by bursting. In a **neg**. sepn. process target-free sample material is recovered following sepn. of the floating layer. The method may also be used diagnostically to detect the presence of a disease marker in a sample. Novel sepn. app. is also described. Perfluorobutane gas microbubbles encapsulated with distearoylphosphatidylserine doped with Mal-PEG2000-distearoylphosphatidylethanolamine (DSPE) was prepd. and reacted with thiolated anti-CD34 antibodies to make a reagent useful for sepg. CD34-**pos**. cells.

L23 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:114928 CAPLUS

DOCUMENT NUMBER: 126:152505

TITLE: The effect of edelfosine on CTP:choline-phosphate cytidylyltransferase activity in leukemic cell lines

AUTHOR(S): Vogler, William R.; Shoji, Mamoru; Hayzer, David J.; Xie, Y. P.; Renshaw, Mary

CORPORATE SOURCE: Division of Hematology/Oncology, Department of Medicine, Emory University, Atlanta, GA, 30322, USA

SOURCE: Leuk. Res. (1996), 20(11/12), 947-951
CODEN: LEREDD; ISSN: 0145-2126

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Analogs of ether **phospholipids** have been shown to have selective anti-**neoplastic** activity. The compds. are known to inhibit **phospholipid** biosynthesis. This paper examines the effect of the alkyl-lysophospholipid, edelfosine, on the rate-limiting enzyme, CTP:choline-phosphate cytidylyltransferase, in de novo phosphatidylcholine synthesis in sensitive and resistant leukemic cell lines. Enzyme activity was measured by the incorporation of 14C-phosphocholine into CDP-choline by lysates of HL60 and K562; cells demonstrated inhibition of incorporation of 14C-phosphocholine in HL60 cell lysates but no inhibition in K562 lysates. Partial purifn. of cytidylyltransferase by SDS-PAGE (SDS-PAGE) and immunoblotting demonstrated similarity between the enzyme isolated from each cell line. Cloning and sequencing of cytidylyltransferase cDNA of HL60 cells was accomplished using a probe encoding the entire **protein** sequence of the K562 cytidylyltransferase gene. A substitution at nucleotide 751 from A in the HL60 cell cDNA clone to G in the K562 cDNA clone resulted in a change in amino acid no. 251 from lysine (**pos.** **charged**) in the HL60 enzyme to glutamic acid (**neg.** **charged**) in the K562 enzyme. This **neg.** **charge** in the lipid-binding domain of the K562 enzyme may result in a weaker binding of edelfosine and the obsd. decrease in activity, as evidenced by resistance to edelfosine by K562 cells.

L23 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:412022 CAPLUS
DOCUMENT NUMBER: 113:12022
TITLE: Disposition characteristics of macromolecules in **tumor**-bearing mice
AUTHOR(S): Takakura, Yoshinobu; Fujita, Takuya; Hashida, Mitsuru; Sezaki, Hitoshi
CORPORATE SOURCE: Kyoto Univ., Kyoto, 606, Japan
SOURCE: Pharm. Res. (1990), 7(4), 339-46
CODEN: PHREEB; ISSN: 0724-8741
DOCUMENT TYPE: Journal
LANGUAGE: English
AB As part of the strategy for the design of macromol. **carriers** for drug targeting, the disposition characteristics of macromols. were studied in mice bearing **tumors** that served as target tissues. Eight kinds of macromols. including four polysaccharides and four **proteins** with different mol. wts. and elec. **charges** were used; tissue distribution and **tumor** localization after i.v. injection were studied. Pharmacokinetic anal. revealed that the tissue radioactivity uptake rate index calcd. in terms of clearance was different among the tested compds.; esp., the urinary radioactivity excretion clearances and the total

hepatic radioactivity uptake clearances varied widely. Compds. with low mol. wts. (approx. 10 kD) or **p s. charges** showed lower **tumor** radioactivity accumulation; radioactivity was rapidly eliminated from the plasma via rapid urinary excretion or extensive hepatic uptake, resp. On the other hand, large and **neg. charged** compds., carboxymethyl dextran, bovine serum albumin, and mouse IgG, showed higher radioactivity accumulation in the **tumor** (calcd. total amts. were 15.6, 10.8, and 20.8% of the dose, resp.) and prolonged retention in the circulation. These results demonstrated that the total systemic exposure rather than the uptake rate index was correlated with total **tumor** uptake. Mol. wt. and elec. **charge** of the macromols. significantly affected their disposition characteristics and, consequently, detd. radioactivity accumulation in the **tumor**. It was concluded that a drug-**carrier** complex designed for system **tumor** targeting should be polyanionic in nature and larger than 70,000 in mol. wt.

L23 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1967:419947 CAPLUS
DOCUMENT NUMBER: 67:19947
TITLE: An alteration of secreted immunoglobulin in serum
AUTHOR(S): Koelsch, Eckehart
CORPORATE SOURCE: Salk Inst. for Biol. Studies, San Diego, Calif., USA
SOURCE: J. Immunol. (1967), 98(4), 854-9
CODEN: JOIMA3
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To show the possible alterations that immunoglobulins might undergo during circulation in the presence of serum enzymes, cells of the myeloma **tumor** MOPC21 of BALB/c mice were incubated for 6 hrs. at 37.degree. with radioactive amino acids. Purified serum myeloma **protein** was added to the incubation fluid as a **carrier**, to ppt. the freshly secreted labeled IgG. Chromatog. on DEAE-Sephadex A-50 with a linear gradient (0.01 to 0.3M) of pH 8.0 phosphate buffer, showed that the labeled IgG was eluted just ahead of the **carrier**. However, 6 days after injection of labeled IgG in normal mice, 3.7% of the radioactivity could be recovered, but was then homogeneously distributed on the **carrier** myeloma **protein**. In **tumor** -bearing mice, only 0.9% of the radioactivity was recovered (higher IgG turnover rate), but it was also distributed on the **carrier**. In vitro the alteration was completed after only 24 hrs. at 37.degree. in normal sterile mouse serum. Electrophoresis on polyacrylamide gel in 4M urea pH 8.4 showed that

IgG was homogeneous, while the **carrier** contained multiple components. From the change in mobility, it appeared that the alteration involved loss of **pos.** or gain of **neg.** **charge**, such as a deamination might produce. Redn. and alkylation of the myeloma **carrier protein** gave stoichiometric amts. of light and heavy chains, showing that the alteration was not a proteolysis.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, CANCERLIT' ENTERED AT 14:46:19 ON 24 APR 2001)

L24 73 S L22
L25 24 S L24 AND (TREAT? OR THERAP? OR PROPHYL?)
L26 18 S L25 NOT L20
L27 12 DUP REM L26 (6 DUPLICATES REMOVED)

L27 ANSWER 1 OF 12 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-205859 [18] WPIDS
DOC. NO. CPI: C2000-063576
TITLE: Epipodophyllotoxin liposomal formulation, uses **phospholipid** and/or sterol solubilizers, does not cause fluid overload, has increased efficiency in **cancer** and proliferative disorders and reduced general toxicity.
DERWENT CLASS: A96 B04 B05
INVENTOR(S): GUPTA, S K; SENGUPTA, S; VELPANDIAN, T
PATENT ASSIGNEE(S): (ALLI-N) ALL INDIA INST MEDICAL SCI
COUNTRY COUNT: 77
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000009071	A2	20000224	(200018)*	EN	54
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 2000016789	A	20000306	(200030)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000009071	A2	WO 1999-IN37	19990810
AU 2000016789	A	AU 2000-16789	19990810

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2000016789 A Based on WO 200009071

PRIORITY APPLN. INFO: IN 1998-2337 19980811
AN 2000-205859 [18] WPIDS
AB WO 200009071 A UPAB: 20000412
NOVELTY - Novel liposomal formulation useful in **treatment** of **cancer** and other proliferative diseases, containing a mixture of at least 0.1-50 mol% of epipodophyllotoxin or its analogs or derivatives, **phospholipids** and/or sterols, both in molar ratio of 1-15.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for processes for their preparation; and a kit containing (I) with cryoprotectants and antioxidants.

ACTIVITY - Anticancer; antiproliferative.

MECHANISM OF ACTION - **Tumor** cells require much nutrient, and attract the liposome formulation. Due to the improved formulation, higher doses of almost insoluble epipodophyllotoxin are introduced into the cells with less dilution. Epipodophyllotoxins inhibit DNA topoisomerase II activity, and block transcription to RNA restricting formation of **proteins** and cell division in **tumor** cells.

USE - The formulation is used in the **treatment** of **cancer** and other proliferative diseases, e.g., psoriasis; particularly small cell lung **cancer**. For convenience, a kit of the formulation is recommended, but antioxidants and cryoprotectants are advisable for storage in this form.

ADVANTAGE - Prior art formulations have required excessive dilution to solubilize the epipodophyllotoxin, with possibility of variable dosage, heart failure, hypertension, hypersensitivity, and body weight loss, as serious side effects. The present formulation is stable, has a lower toxicity profile, a reduced clearance rate, and an increase in AUC over free drug.

Dwg.0/0

L27 ANSWER 2 OF 12 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-042331 [06] WPIDS
CROSS REFERENCE: 2001-042330 [65]
DOC. NO. CPI: C2001-012329
TITLE: New complex for transferring an anionic substance such as a polynucleotide into a cell comprising all or part of the C1 complement factor amino acid sequence, useful to introduce polynucleotides into cells in gene **therapy**.
DERWENT CLASS: B04 D16
INVENTOR(S): JACOB, E
PATENT ASSIGNEE(S): (TRGE) TRANSGENE SA
COUNTRY COUNT: 25

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1052288	A1	20001115	(200106)*	EN	23

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1052288	A1	EP 1999-401155	19990510

PRIORITY APPLN. INFO: EP 1999-401155 19990510
AN 2001-042331 [06] WPIDS
CR 2001-042330 [65]
AB EP 1052288 A UPAB: 20010126
NOVELTY - Complex for transferring an anionic substance e.g. a polynucleotide into a cell comprising at least 1 polypeptide with at least part of the amino acid (aa) sequence of the C1 complement factor (which binds to the anionic substance) and the anionic substance, is new.

USE - The complexes are useful for transferring an anionic substance into a cell (claimed), especially a polynucleotide for gene **therapy** in man and other animals. The complexes may be used for transferring, e.g. a gene enabling permanent/transient expression of a desirable polypeptide, an antisense sequence reducing/blocking undesirable polypeptide production or a sequence encoding an immunogenic polypeptide to invoke humoral and/or cellular responses to infectious agents, **tumor** cells etc. They can also be included (optionally with an **adjuvant** e.g. polyethylene glycol; claimed) in pharmaceutical compositions for transferring an anionic substance into a cell (claimed), which can be administered (e.g. by intramuscular injection, inhalation; claimed) **therapeutically/prophylactically** or for vaccination **treatment** (especially for gene **therapy** ; claimed) to man or other animals as above (claimed).

DESCRIPTION OF DRAWING(S) - The figure shows the efficiency (luciferase activity in relative light units (RLU)/mg **protein**) of complexes C1qA-DNA and K8-DNA versus DNA alone for transferring DNA into 293EBNA cells.

Dwg.1/2

L27 ANSWER 3 OF 12 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-042330 [06] WPIDS
CROSS REFERENCE: 2001-042331 [63]

DOC. NO. CPI: C2001-012328
TITLE: New complex for transferring an anionic substance such as a polynucleotide into a cell comprising all or part of the C1 complement factor amino acid sequence, useful to introduce polynucleotides into cells in gene **therapy**.
DERWENT CLASS: B04 D16
INVENTOR(S): JOCOB, E; JACOB, E; JACOBS, E; BOMPARD, A; VAUTIER, D
PATENT ASSIGNEE(S): (TRGE) TRANSGENE SA
COUNTRY COUNT: 28
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1052287	A2	20001115	(200106)*	EN	19
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
AU 2000032610	A	20001116	(200106)		
CA 2307446	A1	20001110	(200106)	EN	
JP 2001029087	A	20010206	(200111)		46
EP 1052287	A8	20010404	(200120)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1052287	A2	EP 2000-401284	20000508
AU 2000032610	A	AU 2000-32610	20000509
CA 2307446	A1	CA 2000-2307446	20000509
JP 2001029087	A	JP 2000-137647	20000510
EP 1052287	A8	EP 2000-401284	20000508

PRIORITY APPLN. INFO: US 2000-187217 20000303; EP 1999-401155 19990510
AN 2001-042330 [06] WPIDS
CR 2001-042331 [63]
AB EP 1052287 A UPAB: 20010126
NOVELTY - Complex for transferring an anionic substance e.g. a polynucleotide into a cell comprising at least 1 polypeptide with at least part of the amino acid sequence of the C1 complement factor (which binds to the anionic substance) and the anionic substance, is new.

USE - The complexes are useful for transferring an anionic substance into a cell (claimed), especially a polynucleotide for

gene **th rapy** in man and other animals. The method may be used to transfer, e.g. a gene enabling permanent/transient expression of a desirable polypeptide, an antisense sequence reducing/blocking undesirable polypeptide production or a sequence encoding an immunogenic polypeptide to invoke humoral and/or cellular responses to infectious agents, **tumor** cells etc. They can also be included (optionally with an **adjuvant**; claimed) in pharmaceutical compositions for transferring an anionic substance into a cell (claimed), useful **therapeutically/ prophylactically** or for vaccination **treatment** as above (claimed).

DESCRIPTION OF DRAWING(S) - The figure shows the efficiency (luciferase activity in relative light units (RLU)/mg **protein**) of complexes C1qA-DNA and K8-DNA versus DNA alone for transferring DNA into 293EBNA cells.

Dwg.1/2

L27 ANSWER 4 OF 12 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000402986 MEDLINE
DOCUMENT NUMBER: 20372592 PubMed ID: 10910956
TITLE: A potential mechanism for fumonisin B(1)-mediated hepatocarcinogenesis: cyclin D1 stabilization associated with activation of Akt and inhibition of GSK-3beta activity.
AUTHOR: Ramljak D; Calvert R J; Wiesenfeld P W; Diwan B A; Catipovic B; Marasas W F; Victor T C; Anderson L M; Gelderblom W C
CORPORATE SOURCE: Laboratory of Comparative Carcinogenesis, National Cancer Institute, Frederick Cancer Research and Development Center, Building 538, Room 205E, Frederick, MD 21702, USA.. ramljak@mail.ncifcrf.gov
CONTRACT NUMBER: NO1CO56000 (NCI)
SOURCE: CARCINOGENESIS, (2000 Aug) 21 (8) 1537-46. Journal code: C9T; 8008055. ISSN: 0143-3334.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ED Entered STN: 20000901
Last Updated on STN: 20000901
Entered Medline: 20000823

AB Fumonisin B(1) (FB(1)) is a worldwide corn contaminant and has been epidemiologically linked to the high incidence of human esophageal **cancer** in South Africa and China. FB(1) is hepatocarcinogenic in rats by an unknown mechanism. Inhibition of ceramide synthase and disruption of membrane **phospholipids** have been shown to be mechanisms of toxicity. Here we show

overexpression of cyclin D1 **protein** in both preneoplastic and **ne plastic** liver specimens obtained from a long-term feeding study of FB(1) in rats. In rats fed FB(1) short-term, cyclin D1 **protein** levels in liver were increased up to five-fold in a dose-responsive manner. Northern blot analysis demonstrated no increase in mRNA levels of cyclin D1. 2D electrophoresis of cyclin D1 **protein** in FB(1)-**treated** samples showed a distinct pattern of migration (presence of less **negatively charged** form of the **protein**) that differed from controls. Recently, it has been shown that phosphorylation of cyclin D1 by glycogen synthase kinase 3beta (GSK-3beta) on a single threonine residue (Thr-286) **positively** regulates proteosomal degradation of cyclin D1. In FB(1)-**treated** samples we detected GSK-3beta phosphorylated on serine 9; activated **protein** kinase B (Akt) appears to be responsible for this activity-inhibiting phosphorylation. These findings suggest that overexpression of cyclin D1 results from stabilization due to a lack of phosphorylation mediated by GSK-3beta. We also observed an increase in cyclin dependent kinase 4 (Cdk4) complexes with cyclin D1 in FB(1)-**treated** samples; additionally, elevated Cdk4 activity was shown by increased phosphorylation of the retinoblastoma **protein**. In summary, the activation of Akt leads to increased survival, inhibition of GSK-3beta activity and post-translational stabilization of cyclin D1, all events responsible for disruption of the cell cycle G(1)/S restriction point in hepatocytes. This is the first report suggesting the mechanism by which FB(1) acts as a **carcinogen**.

L27 ANSWER 5 OF 12 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-620582 [53] WPIDS
DOC. NO. CPI: C1999-181230
TITLE: Novel contrast agent for ultrasound imaging of subject, particularly myocardium and other tissues.
DERWENT CLASS: B05
INVENTOR(S): CUTHBERTSON, A; ERIKSEN, M; FRIGSTAD, S; OSTENSEN, J; RONGVED, P; SKURTVEIT, R; TOLLESHAUG, H
PATENT ASSIGNEE(S): (ERIK-I) ERIKSEN M; (NYCO-N) NYCOMED IMAGING AS; (MARS-I) MARSDEN J C
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9953963	A1	19991028	(199953)*	EN	80

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK

LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG
SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9936172 A 19991108 (200014)
BR 9909822 A 20001219 (200103)
NO 2000005250 A 20001218 (200106)
EP 1073473 A1 20010207 (200109) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9953963	A1	WO 1999-GB1221	19990422
AU 9936172	A	AU 1999-36172	19990422
BR 9909822	A	BR 1999-9822	19990422
		WO 1999-GB1221	19990422
NO 2000005250	A	WO 1999-GB1221	19990422
		NO 2000-5250	20001019
EP 1073473	A1	EP 1999-918133	19990422
		WO 1999-GB1221	19990422

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9936172	A	Based on	WO 9953963
BR 9909822	A	Based on	WO 9953963
EP 1073473	A1	Based on	WO 9953963

PRIORITY APPLN. INFO: GB 1998-8599 19980422
AN 1999-620582 [53] WPIDS
AB WO 9953963 A UPAB: 19991215
NOVELTY - The contrast agent is formulated by dispersing gas component as a stabilized injectable gas dispersion and the diffusible component as an injectable stabilized oil-in-water emulsion, such that the material present at the surface of the dispersed gas has affinity for the material present at the surface of the dispersed diffusible component.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the method of generating enhanced images of human or non-human animal subject which comprises injecting the aqueous medium into the vascular system of the subject, followed by injecting the oil-in-water emulsion.The emulsion is injected before, during or after injection of the aqueous medium to generate an ultrasound image of at least a portion of the subject.

USE - The contrasting agent is used for ultrasonic visualization of a subject, particularly myocardium and other tissues. Also for imaging other capillary systems such as kidney,

liver, spleen, thyroid, skeletal muscle, breast and prostate. The contrast agent may also be used as delivery agents or as vehicles of **therapeutically** active substances. The contrasting agent may be used **therapeutically** by intervenous injection of a high dose for **treating tumor**, by exposing the **tumor** to local ultrasound irradiation, particularly to **treat** liver, breast, thyroid and prostate **tumours**.

ADVANTAGE - The contrast agent may readily permit effective imaging of tissue such as the myocardium using conventional B- mode scanning techniques. The droplet size of emulsion intended for intravenous injection should be less than 10 mu m, desirably less than 0.1-7 mu m in order to facilitate unimpeded passage through the pulmonary system. If desired, the diffusible component may also be formulated as a micro-emulsions which have good thermodynamic stability. Substantially, lower doses of diffusible component (20 nl diffusible component/kg body weight) containing emulsion can also be used to obtain images comparable to those observed in WO-A-9817324. The diffusible component in the emulsion has the capability of at least 100-fold increase in volume when evaporated, thereby preventing the rise in risk of embolism. The temperature of the dispersed gas and/or emulsion, prior to administration can be manipulated by the use of constituents which react exothermically under the influence of ultrasound radiation, to ensure maximum volatilization of the diffusible component and to enhance growth of the dispersed gas. The exposed gas surface, due to absence of encapsulating material, may cause the contrast agent to exhibit exceptionally favorable acoustic properties due to high backscatter and low energy absorption. The control of the duration of retention of the dispersed gas may be achieved by appropriate adjustment of the dose and/or formulation of the diffusible component, particularly the nature and degree of affinity between the gas component and diffusible component. The effective rate of transport of the diffusible component may be controlled, by adjusting the viscosity of the dispersed gas phase composition and/or the diffusible component composition, by incorporating one or more bio-compatible viscosity enhancers such as X-ray contrast agents, polyethylene glycols, carbohydrate, **proteins**, polymers or alcohols in the formulation. Reduction in the droplets size of the diffusible component will lead to an increase in the overall number of droplets, and so may enhance the rate of transfer by reducing the mean interparticle distance between the gas microbubbles and emulsion droplets, and thus increasing the probability of collision and/or coalescence. Contrast agents containing bio-compatible azeotropic mixtures have effective echogenic lifetime in-vivo, as water solubility, fat solubility, diffusibility and pressure resistivity of the compounds such as fluorocarbons decrease with increasing molecular weight.

Dwg.0/0

L27 ANSWER 6 OF 12 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-633730 [54] WPIDS
DOC. NO. CPI: C1999-185055
TITLE: New conjugate of lipid with basic, membrane-disrupting peptide having reversed amide backbone, used to introduce anionic macromolecules or active agents into cells, e.g. for gene **therapy**.
DERWENT CLASS: B04 D16
INVENTOR(S): KITAS, E A; SCHLAEGER, E
PATENT ASSIGNEE(S): (HOFF) ROCHE DIAGNOSTICS GMBH
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9951629	A2	19991014	(199954)*	EN	23
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9937065	A	19991025	(200011)		
EP 1068225	A2	20010117	(200105)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9951629	A2	WO 1999-EP2361	19990407
AU 9937065	A	AU 1999-37065	19990407
EP 1068225	A2	EP 1999-919208	19990407
		WO 1999-EP2361	19990407

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9937065	A	Based on	WO 9951629
EP 1068225	A2	Based on	WO 9951629

PRIORITY APPLN. INFO: EP 1998-124837 19981230; EP 1998-106302 19980407
AN 1999-633730 [54] WPIDS

AB WO 9951629 A UPAB: 19991221
NOVELTY - Conjugates of (i) lipid and (ii) basic, membrane-disrupting peptides, and their salts, are new.

DETAILED DESCRIPTION - Conjugates of (i) lipids and (ii) basic, membrane-disrupting peptides of formula (I) and their salts, comprise:

R1 and R2 = residues of linear or branched, saturated or unsaturated aliphatic carboxylic acids or **phospholipids**;

R3 = basic, membrane-disrupting peptide with a reversed amide backbone;

Y = 2-10C alkylene;

X = CONH or SS

INDEPENDENT CLAIMS are also included for the following:

(a) the peptide QQRKRKIWSILAPLGTTLVKLVAGIC-NH2 (II) with a reversed amide backbone and with at least 50% of residues D-amino acids, and its derivatives;

(b) compositions containing (I), at least one of helper lipid, short-chain **phospholipid** and/or cationic lipid, optionally also an additional transfection reagent; and

(c) process for introducing into a cell, in vivo or in vitro, an anionic macromolecule (III) or a biologically active anionic molecule (IIIa), by **treating** the cells with (III) or (IIIa) in presence of (I).

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - (I) are used to introduce, into eukaryotic or prokaryotic cells, in vivo or in vitro, anionic macromolecules, particularly nucleic acids, or biologically active anionic molecules. In particular DNA (for gene **therapy** or recombinant **protein** production), antisense sequences, haptamers, triplex-formers, ribozymes etc. also **proteins** and peptides (for immunization) are introduced.

ADVANTAGE - Transfection with (I) provides rapid expression of heterologous **proteins** in large scale systems, with both adherent and suspended cells, even at low DNA concentrations and without significant inhibition by conditioned medium. A conjugate prepared from 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine N-(3-(2-pyridyldithio)propionate and the all D reversed-backbone peptide QQRKRKIWSILAPLGTTLVKLVAGIC-NH2 was formulated with a plasmid encoding the human **tumor** necrosis receptor **protein** p55 and used to transfect HEK293(EBNA) cells. At a conjugate concentration of 10 mg/ml, cell viability was 90-95% with p55 expression 83 ng/ml.

Dwg.0/0

L27 ANSWER 7 OF 12 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-184683 [17] WPIDS
CROSS REFERENCE: 2000-074579 [04]

DOC. NO. CPI: C2000-058046
TITLE: New polyamine telomers useful for gene **therapy**.
DERWENT CLASS: A14 A96 B04 B05 D16
INVENTOR(S): BOUSSIF, O; SANTAELLA, C; VIERLING, P
PATENT ASSIGNEE(S): (TRGE) TRANSGENE SA
COUNTRY COUNT: 25
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 965584	A2	19991222	(200017)*	EN	42

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 965584	A2	EP 1999-111504	19990614

PRIORITY APPLN. INFO: EP 1998-401471 19980615
AN 2000-184683 [17] WPIDS
CR 2000-074579 [04]
AB EP 965584 A UPAB: 20000405
NOVELTY - Polyamine telomers (I) are new.
DETAILED DESCRIPTION - Polyamine telomer of formula (I) are new.
A = H, 1-4C alkyl or 5-7 aryl;
n = 1-100;
R1 = H, methyl, ethyl or -(CH2)u-B1;
x, u = 2-4;
B1 = group of formula (i) or (ii);
y = 2-4;
z = 0-6;
R3-R6 = H, 1-4C alkyl, 1-4C hydroxyalkyl.
INDEPENDENT CLAIMS are also included for:
(1) a composition comprising (I);
(2) a complex for transfering an active substance to a cell comprising at least one (I) and/or at least one of the above composition and at least one active substance (comprising at least one **negative charge**);
(3) tranfering in vitro at least one substance in a cell using the complex;
(4) the preparation of the complex;
(5) a pharmaceutical composition comprising the complex; and
(6) a cell transfected by the complex.

ACTIVITY - None given.

MECHANISM OF ACTION - Transfecting agent for gene **therapy**. A549 cells (epithelial cells derived from human pulmonary **carcinoma**) were cultivated in vitro and **treated** with DNA/telomer complex. 48 hours after transfection the culture medium was removed and washed in order to determine the luciferase activity. The results showed that the polyamines enable transfection of the plasmid into the cells.

USE - (I) are useful for transfering in vitro of at least one nucleic acid in a cell, preferably a mammalian cell. Thus (I) can be useful in composition for vaccinal **treating** or preventing of man and animals, and in gene **therapy** (claimed). The polyamine telomers can also be used for ex vivo or in vivo transfer of nucleic acid into cells.

ADVANTAGE - The polyamines enable transfection of the plasmid into the cells and that the transfection efficiency depends on the length of the polyamine chain, on the **charge** ratio and on the amount of DNA. The presence of an equimolar quantity of DOPE is more efficient than the use of complexes composed of strongly **charged** polyamines (II: L = (iv); m = 17; n = 20, 40 or 60). Dwg.0/5

L27 ANSWER 8 OF 12 MEDLINE

ACCESSION NUMBER:	97217717 MEDLINE
DOCUMENT NUMBER:	97217717 PubMed ID: 9063678
TITLE:	Diversity of lipid-based polyene formulations and their behavior in biological systems.
AUTHOR:	Wasan K M; Lopez-Berestein G
CORPORATE SOURCE:	Division of Pharmaceutics and Biopharmaceutics, Faculty of Pharmaceutical Sciences, University of British Columbia, Canada.
SOURCE:	EUROPEAN JOURNAL OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES, (1997 Jan) 16 (1) 81-92. Ref: 87 Journal code: EM5; 8804297. ISSN: 0934-9723.
PUB. COUNTRY:	GERMANY: Germany, Federal Republic of
	Journal; Article; (JOURNAL ARTICLE)
	General Review; (REVIEW)
	(REVIEW, TUTORIAL)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	199707
ED	Entered STN: 19970721
	Last Updated on STN: 19970721
	Entered Medline: 19970703

AB Patients with **cancer** and infectious disease often display dyslipidemias that result in changes in their plasma lipoprotein-lipid composition. It is likely that the interactions of

liposomal polyenes with plasma lipoproteins may be responsible for the far different pharmacokinetics and pharmacodynamics of these compounds when they are administered to infected patients rather than to animals or healthy volunteers. Amphotericin B (AmpB) and nystatin are examples of such polyenes. Amphotericin B initially distributes with the high-density lipoprotein (HDL) fraction upon incubation in plasma. Over time, AmpB redistributes from HDLs to low-density lipoproteins (LDLs). This redistribution appears to be regulated by lipid transfer **protein**. However, when AmpB is incorporated into liposomes composed of **negatively** or **positively charged phospholipids**, not only is the capability of LTP to transfer AmpB from HDL to LDL diminished, but AmpB remains retained with only the HDL fraction. However, when liposomal nystatin is incubated in plasma, over 50% of nystatin distributes with HDLs. Over time, nystatin redistributes from HDL to the lipoprotein-deficient plasma fraction, which is composed of mainly aqueous plasma **proteins**. The lipid composition selected for the drug appears to be a vital constituent in regulating the drug's interaction with biological fluids. Furthermore, liposome (or liposomal particle) size, fluidity, and other physiochemical characteristics also play a role in altering the pharmacokinetics and pharmacological effects of lipid-based drug formulations. Armed with this understanding, a rational approach to clinical development of these formulations could be facilitated.

L27 ANSWER 9 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1997:113034 BIOSIS
DOCUMENT NUMBER: PREV199799412237
TITLE: The effect of edelfosine on CTP: Cholinephosphate cytidylyltransferase activity in leukemic cell lines.
AUTHOR(S): Vogler, William R. (1); Shoji, Mamoru; Hayzer, David J.; Xie, Y. P.; Renshaw, Mary
CORPORATE SOURCE: (1) Suite 500, 1100 Lake Hearn Drive, Atlanta, GA 30342 USA
SOURCE: Leukemia Research, (1996) Vol. 20, No. 11-12, pp. 947-951.
ISSN: 0145-2126.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Analogs of ether **phospholipids** have been shown to have selective anti-**neoplastic** activity. The compounds are known to inhibit **phospholipid** biosynthesis. This paper examines the effect of the alkyl-lysophospholipid, edelfosine, on the rate-limiting enzyme, CTP:choline-phosphate cytidylyltransferase, in de novo phosphatidylcholine synthesis in sensitive and resistant leukemic cell lines. Enzyme activity was measured by the incorporation of 14C-phosphocholine into CDP-choline by lysates of HL60 and K562; cells demonstrated inhibition of

incorporation of 14C-phosphocholine in HL60 cell lysates but no inhibition in K562 lysates. Partial purification of cytidylyltransferase by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and immunoblotting demonstrated similarity between the enzyme isolated from each cell line. Cloning and sequencing of cytidylyltransferase cDNA of HL60 cells was accomplished using a probe encoding the entire **protein** sequence of the K562 cytidylyltransferase gene. A substitution at nucleotide 751 from A in the HL60 cell cDNA clone to G in the K562 cDNA clone resulted in a change in amino acid number 251 from lysine (**positively charged**) in the HL60 enzyme to glutamic acid (**negatively charged**) in the K562 enzyme. This **negative charge** in the lipid-binding domain of the K562 enzyme may result in a weaker binding of edelfosine and the observed decrease in activity, as evidenced by resistance to edelfosine by K562 cells.

L27 ANSWER 10 OF 12 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 90373925 MEDLINE
DOCUMENT NUMBER: 90373925 PubMed ID: 2204445
TITLE: Ambazone as a membrane active antitumor drug.
AUTHOR: Lober G; Hoffmann H
CORPORATE SOURCE: Central Institute of Microbiology and Experimental Therapy, Academy of Sciences of the G.D.R., Jena.
SOURCE: BIOPHYSICAL CHEMISTRY, (1990 Apr) 35 (2-3) 287-300.
Ref: 56
Journal code: A5T; 0403171. ISSN: 0301-4622.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199010
ED Entered STN: 19901122
Last Updated on STN: 19901122
Entered Medline: 19901018

AB Ambazone (1,4-benzoquinone guanylhydrazone thiosemicarbazone) was found to be active against various transplantable **tumors** in mice as well as rats. When administered orally for 4-9 days, the effective **therapeutic** dose ranged between 60 and 125 mg/kg. The antineoplastic effect of ambazone appeared to be mediated, at least in part, by the immune system. In order to characterize the drug, biophysical and biophysicochemical studies were carried out using thin-layer chromatography, absorption spectroscopy and polarographic measurements. The distribution of ambazone in an n-octanol/water system indicated low hydrophobicity, thereby excluding the possibility of a preferential contribution

from hydrophobic forces to the mode of action of ambazone. Ambazone undergoes three protonation reactions with pK values at 10.69 (equilibrium between the **negatively charged** and neutral forms), 7.39 (equilibrium between the neutral and singly **positively charged** form) and 6.22 (equilibrium between the singly and doubly **positively charge** form). Interaction of the drug with model membrane system was monitored by spectrophotometric and fluorescence measurements. Using the fluorescence label 1-anilino-8-naphthalenesulfonic acid (ANS) as a probe pointed to the interaction of ambazone with the inner area of the **phospholipid** bilayer matrix of liposomes as being nonspecific. Ambazone induces an overall increase in the cellular cAMP content of leukemia cells and macrophages. So far, membrane interaction has provided a molecular basis for both immunological and antineoplastic activities of the drug. By performing DNA melting experiments, it was shown that neutral or singly **positively charged** ambazone species stabilize the secondary structure of DNA, while the doubly **positively charged** form binds more strongly and destabilizes the DNA. After oral administration to rats and mice, ambazone was found to be incompletely absorbed from the gastrointestinal tract, to an extent of about 35-50%. Absorbed ambazone binds only weakly to plasma **proteins**, whereas its binding to red blood cells is relatively strong. The mutagenic potential of ambazone shown in bacterial systems and human lymphocytes corresponds to its relatively weak interaction with DNA. The toxic action of ambazone on the intestine is believed to be due to inhibition by the drug of bacterial DNA, RNA and **protein** syntheses. It is assumed that the reported affinity of ambazone for different cellular targets, i.e., membranes, nucleic acids and **proteins**, contributes to the overall antibacterial effect. The weak antiviral activity of ambazone in the Sendai virus/chicken embryo fibroblast system is probably the result of the interaction with Sendai virus NH glycoprotein.

L27 ANSWER 11 OF 12 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1989-167174 [23] WPIDS
DOC. NO. CPI: C1989-074190
TITLE: Adsorbent for beta 2-micro globulin - comprises poly-amino acid, polysaccharide, synthetic high polymer, collagen or gelatin on water insoluble **carrier**.
DERWENT CLASS: A96 B04 P34
INVENTOR(S): WATANABE, H; YAMAWAKI, N; YOKOYAMA, T
PATENT ASSIGNEE(S): (ASAH) ASAHI KASEI KOGYO KK; (ASAH) ASAHI MEDICAL CO LTD
COUNTRY COUNT: 13
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 319144	A	19890607	(198923)*	EN	28
R: AT BE CH DE ES FR GB IT LI NL SE					
JP 01124468	A	19890517	(198926)		
JP 02045065	A	19900215	(199013)		
JP 02052669	A	19900222	(199014)		
US 5051185	A	19910924	(199141)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 319144	A	EP 1988-310352	19881103
JP 01124468	A	JP 1987-279376	19871106
JP 02045065	A	JP 1988-196197	19880808
JP 02052669	A	JP 1988-203776	19880818
US 5051185	A	US 1990-512629	19900419

PRIORITY APPLN. INFO: JP 1987-279376 19871106; JP 1988-196197 19880808; JP 1988-203776 19880818

AN 1989-167174 [23] WPIDS

AB EP 319144 A UPAB: 19930923

An adsorbent for beta2-microglobin (BM) comprises a water-insol. **carrier** support, as a ligand, at least one electrolyte selected from a polyamino acid, a polysaccharide, a synthetic high polymer, collagen having an isoelectric point of 9.5 or more and gelatin having an isoelectric point of 6.5 or more. The electrolyte has a mol. wt. not less than 1,000 and an X value of more than 2, where X is a relationship regarding the skeleton structure of the electrolyte and is the sum of A and B, where A is (the number of C atoms of the skeleton structure) - (the number of hydrophilic gps)/(the number of hydrophilic gps.) and B is (the number of cationic gps) - (the number of anionic gps)/ (the number of hydrophilic gps.).

Suitable electrolytes are e.g. poly(glutamic acid-alanine), poly (glutamic acid-alanine-tyrosine), diethylaminoethyl-dextran, sodium sulphonated polystyrene, styrene-maleic acid copolymer, methylated atelocollagen type I or gelatin, obtd. by heat **treatment** of collagen under acid conditions. The **carrier** is pref. 2-hydroxyethyl methacrylate-diethylaminoethyl, methacrylate copolymer. The **carrier** may be activated using an epoxide e.g. epichlorohydrin.

USE/ADVANTAGE - The adsorbent can be used for selectively adsorbing BM at high efficiency without involving nonspecific adsorption of other useful **proteins**, partic. albumin. It

can be used for cleaning body fluids (e.g. blood) for removing BM which is found in high levels in body fluids of patients suffering from renal insufficiency or malignant **tumour** and causes flexor canal syndrome, amyloidosis, digitus recellens, gonalgia, pruritis and bone involvement.

0/2

ABEQ US 5051185 A UPAB: 19930923

A specific selective absorbent for beta 2 microglubulin comprises a water-insol. carier supporting as ligand electrolyte(s) selected from polyamino acid, polysaccharide, synthetic high polymer, a collagen of isoelectric pt. 9.5+ or gelatin of isoelectric pt. 6.5+. The electrolyte contains gp(s) with **positive** and **negative charges** in neutral non-electrolyte soln. has M.W. 1000+ and X value above 2.0 X is A + B where A is (No. of C atoms of skeletal structure)-(N0. of hydrophilic gps)/(No. of hydrophobic gps.) and B is (No. of anionic gps)/(No. of hydrophilic gps.).

Pref. electrolytes are polyamino acids, polysaccharides or synthetic high polymers pref. the ligand has M.W. 10 power 3 - 10 power 6 with X value 2-15. Typical polyamino acids are poly(glutaric acid-alanine) and poly(glutaric acid-alanine-tyrosine). A typical polysaccharides is diethylaminoethyl dextran and typical synthetics are Na sulphonated polystyrene or styrene-maleic acid copolymer.

USE - The cleaning and regeneration of body fluids (blood, plasma, serum, ascites, hydrothorax of patients with renal insufficiency or **tumours** by selective removal or beta 2 micro-globulin without taking out albumin or posing a need for replacement of body fluids. @

L27 ANSWER 12 OF 12 CANCERLIT

ACCESSION NUMBER: 85609630 CANCERLIT
DOCUMENT NUMBER: 85609630
TITLE: RECEPTOR-MEDIATED ENDOCYTOSIS BY NORMAL AND PROLIFERATING HEPATOCYTES AND LIPOSOMAL DRUG DELIVERY.
AUTHOR: Wolkoff A W; Stockert R J; Schein P S
CORPORATE SOURCE: Liver Res. Center, Albert Einstein Coll. of Medicine, 1300 Morris Park, Bronx, New York, NY 10461.
SOURCE: Dev Oncol, (1984). Vol. 24, pp. 278-91.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 198507

AB A specific liver cell membrane receptor, hepatic binding **protein** (HBP), is necessary for the uptake of asialoglycoproteins by hepatocytes. Isolated perfused rat liver pre-infused with anti-HBP IgG exhibited 80% reduction in asialoorosomucoid (ASOR) uptake, but no change in bilirubin uptake,

when these substances were injected into the portal vein. Specific inhibitors have been found that affect steps in the endocytosis of ASOR following binding to HBP. In studies using perfused regenerating rat liver, uptake of radiolabeled bilirubin and ASOR fell by over 50% and 80%, respectively, reaching a nadir at the time of greatest cell proliferation. **Treatment** with nafenopin, although it induced a 40% increase in liver wt 24 hr after 2 days of **treatment**, did not result in changes in transport of bilirubin or ASOR, indicating that hepatocellular proliferation alone is not responsible for the observed alterations in transport. HBP content measurements in rat liver following exposure to N-2-acetylaminofluorene showed that HBP in dissected **neoplastic** nodules was reduced by almost 70% in **neoplastic** nodules and 95% in areas of hepatocellular **carcinoma** (125I-ASOR assay for HBP). Cells of the undifferentiated human hepatocellular **carcinoma** line PLC/PRF/5, which lacks HBP, were killed by methotrexate, both in the presence and absence of an asialofetuin-folinic acid conjugate, a methotrexate antagonist that binds to receptor-bearing cells; in contrast, the more differentiated human hepatocellular **carcinoma** line, HepG2, which expresses HBP, could be spared from methotrexate-mediated killing by the presence of the asialofetuin-folinic acid conjugate in the medium. Incorporation of adriamycin into **positively charged** liposomes was found to effectively retard the in vivo uptake of this cardiotoxic drug into mouse cardiac muscle, relative to the uptake of free drug or of the drug incorporated into **negatively charged** liposomes; these findings and others reported suggested that liposomes may be developed that can deliver their contents to specific cell types by targeting them to particular cell surface receptors. (30 Refs)

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, CANCERLIT' ENTERED AT 14:51:15 ON 24 APR 2001)

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L28       10566 S COX J?/AU                    - Author (5)
L29          82 S DRANE D?/AU
L30         300 S SUHRBIER A?/AU
L31           0 S L28 AND L29 AND L30
L32          39 S L28 AND (L29 OR L30)
L33           4 S L29 AND L30
L34       10905 S L28 OR L29 OR L30
L35          97 S L34 AND L10
L36           2 S L35 AND CHARGE#
L37          43 S L32 OR L33 OR L36
L38          15 DUP REM L37 (28 DUPLICATES REMOVED)

L38  ANSWER 1 OF 15  CAPLUS  COPYRIGHT 2001 ACS        DUPLICATE 1
ACCESSION NUMBER:        2001:167132  CAPLUS
```

TITLE: Characterization of hepatitis C virus core-specific immune responses primed in rhesus macaques by a nonclassical ISCOM vaccine

AUTHOR(S): Polakos, Noelle K.; **Drane, Debbie**; **Cox, John**; Ng, Philip; Selby, Mark J.; Chien, David; O'Hagan, Derek T.; Houghton, Michael; Paliard, Xavier

CORPORATE SOURCE: Chiron Corp., Emeryville, CA, 94608, USA

SOURCE: J. Immunol. (2001), 166(5), 3589-3598
CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Current therapies for the treatment of hepatitis C virus (HCV) infection are only effective in a restricted no. of patients. Cellular immune responses, particularly those mediated by CD8+ CTLs, are thought to play a role in the control of infection and the response to antiviral therapies. Because the Core protein is the most conserved HCV protein among genotypes, we evaluated the ability of a Core prototype vaccine to prime cellular immune responses in rhesus macaques. Since there are serious concerns about using a genetic vaccine encoding for Core, this vaccine was a nonclassical ISCOM formulation in which the Core protein was adsorbed onto (not entrapped within) the ISCOMA TRIX, resulting in .apprx.1-.mu.m particulates (as opposed to 40 nm for classical ISCOM formulations). We report that this Core-ISCOM prototype vaccine primed strong CD4+ and CD8+ T cell responses. Using intracellular staining for cytokines, we show that in immunized animals 0.30-0.71 and 0.32-2.21% of the circulating CD8+ and CD4+ T cells, resp., were specific for naturally processed HCV Core peptides. Furthermore, this vaccine elicited a Th0-type response and induced a high titer of Abs against Core and long-lived cellular immune responses. Finally, we provide evidence that Core-ISCOM could serve as an adjuvant for the HCV envelope protein E1E2. Thus, these data provide evidence that Core-ISCOM is effective at inducing cellular and humoral immune responses in nonhuman primates.

REFERENCE COUNT: 27

REFERENCE(S):

(2) Ballardini, G; J Clin Invest 1995, V95, P2067 CAPLUS
(4) Calabrese, F; Hepatology 2000, V31, P1153 CAPLUS
(5) Choo, Q; Proc Natl Acad Sci USA 1991, V88, P2451 CAPLUS
(6) Cohen, J; Science 1999, V285, P26 CAPLUS
(7) Cooper, S; Immunity 1999, V10, P439 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2

ACCESSION NUMBER: 2001:207147 CAPLUS
TITLE: Immune responses to ISCOM.RTM. formulations in animal and primate models
AUTHOR(S): Sjolander, A.; **Drane, D.**; Maraskovsky, E.; Scheerlinck, J.-P.; **Suhrbier, A.**; Tennent, J.; Pearse, M.
CORPORATE SOURCE: Immunology Department, CSL Limited, Melbourne, 3052, Australia
SOURCE: Vaccine (2001), 19(17-19), 2661-2665
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB ISCOMs.RTM. are typically 40 nm cage-like structures comprising antigen, saponin, cholesterol and phospholipid. ISCOMs.RTM. have been shown to induce antibody responses and activate T helper cells and cytolytic T lymphocytes in a no. of animal species, including non-human primates. Recent clin. studies have demonstrated that ISCOMs.RTM. are also able to induce antibody and cellular immune responses in humans. This review describes the current understanding of the ability of ISCOMs.RTM. to induce immune responses and the mechanisms underlying this property. Recent progress in the characterization and manuf. of ISCOMs.RTM. will also be discussed.

L38 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3
ACCESSION NUMBER: 2000:592580 CAPLUS
DOCUMENT NUMBER: 133:191986
TITLE: Immunogenic complexes and methods relating thereto
INVENTOR(S): **Cox, John Cooper; Drane, Debbie Pauline**
PATENT ASSIGNEE(S): CSL Limited, Australia
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000048630	A1	20000824	WO 2000-AU110	20000217

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,

VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 1999-8735 A 19990217
AU 1999-1861 A 19990727

AB The present invention relates generally to an immunogenic complex comprising a **charged** org. **carrier** and a **charged antigen** and, more particularly, a neg. **charged** org. **carrier** and a pos. **charged antigen**. The complexes of the present invention are useful, inter alia , as therapeutic and/or prophylactic agents for facilitating the induction of a cytotoxic T-lymphocyte response to an **antigen**.

REFERENCE COUNT: 5

REFERENCE(S):
(1) Callahan, P; Pharmaceutical Research 1991, V8(7), P851 CAPLUS
(2) Friede, M; Molecular Immunology 1993, V30(6), P539 CAPLUS
(3) Morein; EP 0109942 A 1984 CAPLUS
(4) Morein; EP 0180564 A 1986 CAPLUS
(5) Nakanishi, T; Biochemical and Biophysical Research Communications 1997, V240(3), P793 CAPLUS

L38 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 4

ACCESSION NUMBER: 1999:253116 CAPLUS
DOCUMENT NUMBER: 131:86619
TITLE: Peptide based cytotoxic T-cell vaccines; delivery of multiple epitopes, help, memory and problems
AUTHOR(S): Elliott, Suzanne L.; Pye, Stephanie; Le, Thuy; Mateo, Luis; **Cox, John**; Macdonald, Lisa; Scalzo, Anthony A.; Forbes, Cathy A.; **Suhrbier, Andreas**
CORPORATE SOURCE: Co-operative Research Centre for Vaccine Technology, Queensland Institute of Medical Research, PO Royal Brisbane Hospital, Brisbane, 4029, Australia
SOURCE: Vaccine (1999), 17(15-16), 2009-2019
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Synthetic CD8+ cytotoxic T-lymphocyte (CTL) peptide epitope based vaccines are being developed against a no. of human diseases. Here we describe extensive preclin. testing of peptide epitope vaccines formulated with a protein as a source of CD4 help and Montanide ISA

720, an adjuvant currently in human clin. trials. Such water-in-oil formulations could effectively co-deliver several peptide epitopes and simultaneously induce multiple independent CTL responses. The efficiency of CTL induction by some peptides was, however, dependent on the aq. buffer conditions, with poor performance correlating with non-covalent peptide oligomerization. Any of a no. of proteins currently used in human vaccines could supply CD4 help and no difference in CTL induction was obtained if the CD4 response was amnestic or a primary. Peptide immunization was found to induce long term CTL memory and the recall of protective responses did not depend on an amnestic CD4 response. Slow pyroglutamic acid formation and rapid oxidn. of methionine residues was obsd. in water-in-oil formulations, however, the latter had no effect on CTL induction. These data highlight the need to monitor for potential deleterious chem. events and interpeptide interactions, but illustrate that peptide based vaccination can effectively deliver multiple epitopes, in conjunction with any protein, and induce protective memory.

REFERENCE COUNT: 47

REFERENCE(S):
(1) Adorini, L; Immunol Today 1990, V11, P21 CAPLUS
(3) Ahmed, R; Science 1996, V272, P54 CAPLUS
(4) Bennett, S; J Exp Med 1997, V186, P65 CAPLUS
(5) Boyer, J; Nat Med 1997, V3, P526 CAPLUS
(6) Chen, W; J Immunol 1996, V157, P1000 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 5 OF 15 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1998347307 MEDLINE
DOCUMENT NUMBER: 98347307 PubMed ID: 9682385
TITLE: Studies on experimental adjuvanted influenza vaccines: comparison of immune stimulating complexes (Iscoms) and oil-in-water vaccines.
AUTHOR: Coulter A; Wong T Y; **Drane D**; Bates J; Macfarlan R; **Cox J**
CORPORATE SOURCE: CSL Limited, Parkville, Victoria, Australia.
SOURCE: VACCINE, (1998 Jul) 16 (11-12) 1243-53. Journal code: X60; 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ED Entered STN: 19981029
Last Updated on STN: 19981029
Entered Medline: 19981022

AB Detergent-disrupted influenza virus vaccines, formulated as Iscoms, or oil-in-water (o/w) emulsions, were administered parenterally to

mice and evaluated for immunogenicity and protective efficacy. Both formulations enhanced both primary and secondary serum antibody responses. The magnitude of these responses with o/w emulsions was further enhanced by the addition of the non-ionic block copolymer L121 in the emulsion. Four weeks after primary immunization, mice were challenged by exposure to an aerosol containing infectious virus. Resistance to challenge in terms of survival rate and weight change correlated well with serum antibody titre for all formulations. Two major differences were observed between the adjuvant formulations. Iscom vaccines, formulated with Quil-A or the less toxic Quillaia saponin preparation Iscoprep 703, induced specific cytotoxic T-lymphocyte responses, whereas the o/w-based vaccines did not. In addition, dose-site reactivity studies in sheep showed that Iscom vaccines were less reactive than o/w-based vaccines, the degree of reactivity of the latter increasing sharply with increasing L121 concentration. On the basis of these studies, Iscoms were chosen for development as a potential adjuvant for human influenza vaccines.

L38 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:555272 CAPLUS
DOCUMENT NUMBER: 129:314683
TITLE: Development of an influenza-Iscom vaccine
AUTHOR(S): **Cox, John**; Coulter, Alan; Macfarlan, Rod; Beezum, Lorraine; Bates, John; Wong, Tuen-Yee; **Drane, Debbie**
CORPORATE SOURCE: CSL Ltd., Victoria, 3052, Australia
SOURCE: NATO ASI Ser., Ser. A (1997), 293(Vaccine Design), 33-49
CODEN: NALSDJ; ISSN: 0258-1213
PUBLISHER: Plenum Publishing Corp.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors describe their rationale for chosing certain adjuvants with the potential to improve the efficacy of a human influenza vaccine. They provide an overview of initial evaluative studies in mice and the optimization steps for Iscoms.

L38 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:87807 CAPLUS
DOCUMENT NUMBER: 126:176738
TITLE: Iscom adjuvant. A promising adjuvant for influenza virus vaccines
AUTHOR(S): Bates, J.; Ackland, J.; Coulter, A.; **Cox, J.**; **Drane, D.**; Macfarlan, R.; Varigos, J.; Wong, T-Y.; Woods, W.
CORPORATE SOURCE: Research and Development, CSL Limited, Parkville, Australia

SOURCE: Int. Congr. Ser. (1996), 1123(Options for the Control of Influenza III), 661-667
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Immunostimulating complexes (Iscoms) enhance the immunogenicity of many antigens and induce both humoral and cell mediated immune responses in animal models. Data generated in mice showed that Iscom adjuvant influenza virus vaccines induce enhanced-humoral and cell-mediated immune responses. These enhanced responses greatly increased the protective efficacy of these vaccines. Enhanced humoral immune responses have also been demonstrated in sheep. The adjuvant alone (Iscomatrix) was well tolerated in healthy young adult volunteers.

L38 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 6

ACCESSION NUMBER: 1995:978850 CAPLUS
DOCUMENT NUMBER: 124:7062

TITLE: Vaccine formulation for use in inducing cytotoxic T lymphocytes

INVENTOR(S): **Cox, John Cooper**; **Suhrbier, Andreas**; Elliott, Suzanne Louise
PATENT ASSIGNEE(S): Council of the Queensland Institute of Medical Research, Australia; Commonwealth Scientific and Industrial Research Organization; University of Melbourne; Walter and Eliza Hall Institute of Medical Research; Biotech Australia Pty. Ltd.; CSL Ltd.

SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9524926	A1	19950921	WO 1995-AU141	19950316
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2185540	AA	19950921	CA 1995-2185540	19950316
CA 2185541	AA	19950921	CA 1995-2185541	19950316

AU 9519426	A1	19951003	AU 1995-19426	19950316
AU 9893289	A1	19990128	AU 1998-93289	19981119
AU 724248	B2	20000914		

PRIORITY APPLN. INFO.: AU 1994-4465 A 19940316
AU 1995-19425 A3 19950316
WO 1995-AU141 W 19950316

AB The present invention provides a compn. where a CTL peptide is presented in such a way as to maximize the attachment of peptide to class 1 MHC mols. on the external surface of cells and the subsequent processing of these cells in the optimal way to induce high-affinity CD8+ CTL responses. Preferably, the compn. comprises a water-in-oil formulation including at least one antigen to which the individual will mount an anamnestic response and at least one cytotoxic T-cell epitope. The antigen is selected from the group consisting of tetanus toxoid, diphtheria toxoid, Bordetella pertussis antigens, poliovirus antigens, helper epitopes and combinations. The T cell epitope is derived from Epstein-Barr virus and is selected from QAKWRLQTL, RYSIFFDY, HLAAQGMAY, YPLHEQHGM, SVRDRLARL, AVLLHEESM, VSFIEFVGW, FRKAQIQGL, PYLFWLAAI, TVFYNIPPMPL, PGDQLPGFSDGRACPV, VEITPYKPTW, AND FLRGRAYGL.

L38 ANSWER 9 OF 15 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1995-336817 [43] WPIDS
CROSS REFERENCE: 1995-336818 [43]
DOC. NO. CPI: C1995-148505
TITLE: New cytotoxic T-cell epitope(s) of Epstein Barr virus - useful in sub-unit vaccines to induce cytotoxic T cells.
DERWENT CLASS: B04
INVENTOR(S): BURROWS, J M; BURROWS, S R; KERR, B M; KHANNA, R; MOSS, D J; **SUHRBIER, A; COX, J C**
; ELLIOTT, S L; SUHRIBIER, A
PATENT ASSIGNEE(S): (BIOT-N) BIOTECH AUSTRALIA PTY LTD; (CSIR) COMMONWEALTH SCI & IND RES ORG; (COUN-N) COUNCIL QUEENSLAND INST MEDICAL RES; (CSLC-N) CSL LTD; (HALL-N) HALL INST MEDICAL RES`WALTER & ELIZA; (UYME) UNIV MELBOURNE
COUNTRY COUNT: 62
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9524925	A1	19950921	(199543)*	EN	23

RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NL NO NZ PL PT RO RU SD SE SG SI SK TJ TT UA US UZ VN

AU 9519425	A	19951003 (199602)	
GB 2301591	A	19961211 (199702)	1
JP 10501682	W	19980217 (199817)	25
GB 2301591	B	19980527 (199823)	
NZ 282348	A	19980527 (199827)	
US 5869453	A	19990209 (199913)	
AU 9893289	A	19990128 (199916)#	
AU 724248	B	20000914 (200051)#	

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9524925	A1		WO 1995-AU140	19950316
AU 9519425	A		AU 1995-19425	19950316
GB 2301591	A		WO 1995-AU140	19950316
			GB 1996-19232	19960913
JP 10501682	W		JP 1995-523739	19950316
			WO 1995-AU140	19950316
GB 2301591	B		WO 1995-AU140	19950316
			GB 1996-19232	19960913
NZ 282348	A		NZ 1995-282348	19950316
			WO 1995-AU140	19950316
US 5869453	A		WO 1995-AU140	19950316
			US 1997-704655	19970127
AU 9893289	A	Div ex	AU 1995-19425	19950316
			AU 1998-93289	19981119
AU 724248	B	Div ex	AU 1995-19425	19950316
			AU 1998-93289	19981119

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9519425	A	Based on	WO 9524925
GB 2301591	A	Based on	WO 9524925
JP 10501682	W	Based on	WO 9524925
GB 2301591	B	Based on	WO 9524925
NZ 282348	A	Based on	WO 9524925
US 5869453	A	Based on	WO 9524925
AU 724248	B	Previous Publ.	AU 9893289

PRIORITY APPLN. INFO: AU 1994-4465 19940316; AU 1998-93289 19981119

AN 1995-336817 [43] WPIDS

CR 1995-336818 [43]

AB WO 9524925 A UPAB: 20001016

The cytotoxic Epstein-Barr virus (EBV) T-cell epitopes of formula

(1)-(12), and their variants, are new: QAKWRLQTL (1), RYSIFFDY (2), HLAAQGMAY (3), YPLHEQHGM (4), SVRDRLARL (5), AVLLHEESM (6), VSFIEFVGW (7), FRKAQIQGL (8), PYLFWLAAI (9), TVFYNIPPMPL (10), PGDQLPGFSDGRACPV (11), VEITPYKPTW (12).

USE - These epitopes are used to induce cytotoxic T lymphocytes (CTL) in a subject, i.e. they are components of subunit vaccines partic. useful against viral infections where CD8+ CTL are protective.

ADVANTAGE - These epitopes are small, stable peptides that are easy to make without involving any infectious material. They should provide vaccines without any oncogenic potential (contrast vaccines based on full length latent antigen proteins).

Dwg.0/3

L38 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 7

ACCESSION NUMBER: 1995:335985 CAPLUS
DOCUMENT NUMBER: 122:130844
TITLE: Induction of protective cytotoxic T cells to murine cytomegalovirus by using a nonapeptide and a human-compatible adjuvant (Montanide ISA 720)
AUTHOR(S): Scalzo, Anthony A.; Elliott, Suzanne L.; **Cox, John**; Gardner, Joy; Moss, Denis J.; **Suhrbier, Andreas**
CORPORATE SOURCE: Dep. Microbiol., Univ. Western Australia, Nedlands, 6009, Australia
SOURCE: J. Virol. (1995), 69(2), 1306-9
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The use of synthetic peptides representing cytotoxic T-cell (CTL) epitopes for human vaccination requires the identification of a suitable adjuvant formulation. A single immunization with Montanide ISA720/tetanus toxoid/YPHFMPTNL protected mice against murine cytomegalovirus and induced epitope-specific CTL. Such formulations will find application in peptide-based CTL anti-viral vaccines.

L38 ANSWER 11 OF 15 MEDLINE DUPLICATE 8

ACCESSION NUMBER: 95187702 MEDLINE
DOCUMENT NUMBER: 95187702 PubMed ID: 7881899
TITLE: Negative staining can cause clumping of Bordetella pertussis fimbriae.
AUTHOR: Hamilton R C; Bennet J; **Drane D**; Pietrzykowski E; Seddon F; Stefancic A; **Cox J**
CORPORATE SOURCE: Research and Development Division, CSL Ltd., Parkville, Victoria, Australia.
SOURCE: MICRON, (1994) 25 (6) 613-5.
Journal code: B3V; 9312850. ISSN: 0968-4328.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
ED Entered STN: 19950425
Last Updated on STN: 19950425
Entered Medline: 19950407

AB The state of fimbriae type 2 (Fim 2) and fimbriae type 3 (Fim 3) preparations from Bordetella pertussis were examined by negative stain electron microscopy. Uranyl acetate induced clumping of Fim 3 regardless of pH and was unsuitable as a stain for establishing the state of fimbriae. Both ammonium molybdate and sodium phosphotungstate were able to show the differences in Fim 3 stored at pH 7.2 and pH 9.5.

L38 ANSWER 12 OF 15 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 95065550 MEDLINE
DOCUMENT NUMBER: 95065550 PubMed ID: 7975154
TITLE: Evaluation of a novel diagnostic test for canine parvovirus.
AUTHOR: **Drane D P**; Hamilton R C; **Cox J C**
CORPORATE SOURCE: Research and Development Division, CSL Limited, Parkville, Vic., Australia.
SOURCE: VETERINARY MICROBIOLOGY, (1994 Aug 1) 41 (3) 293-302.
Journal code: XBW; 7705469. ISSN: 0378-1135.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ED Entered STN: 19950110
Last Updated on STN: 19970203
Entered Medline: 19941229

AB The CPV ELISA detection kit (CSL Ltd., Melbourne Australia) was developed as a rapid field test for the detection of canine parvovirus (CPV) antigen in canine faecal samples. The kit utilises a novel concept in enzyme immunoassay (ELISA) where the conjugate is lyophilised along with the solid-phase capture antibody in the test well. The CPV ELISA was compared to the haemagglutination assay (HA) test using electron microscopy (EM) and/or virus isolation (VI) to confirm infection. The CPV ELISA had a sensitivity of 87% and a specificity of 100% compared to 87% and 63% respectively for the HA. The poor specificity of the HA results in a low positive predictive value of 51% compared to 100% for the CPV ELISA. The CPV ELISA requires no specialised equipment, is simple to perform and provides a visible result in less than 15 minutes.

L38 ANSWER 13 OF 15 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93266446 EMBASE
DOCUMENT NUMBER: 1993266446
TITLE: The development and validation of antigen and antibody assays B. pertussis.
AUTHOR: Bennet J.; **Drane D.**; Pietrzykowski E.; Stefancic A.; Seddon F.; **Cox J.**
CORPORATE SOURCE: CSL Ltd,Parkville, Vic. 3052, Australia
SOURCE: Biologicals, (1993) 21/1 (43).
ISSN: 1045-1056 CODEN: BILSEC
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
007 Pediatrics and Pediatric Surgery
015 Chest Diseases, Thoracic Surgery and Tuberculosis
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English

L38 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 10
ACCESSION NUMBER: 1992:229687 CAPLUS
DOCUMENT NUMBER: 116:229687
TITLE: A novel format for a rapid sandwich EIA and its application to the identification of snake venoms
AUTHOR(S): **Cox, John C.**; Moisidis, Anastasia V.; Shepherd, Jane M.; **Drane, Debbie P.**; Jones, Stephen L.
CORPORATE SOURCE: Res. Dev. Div., Commonw. Serum Lab. Ltd., Parkville, 3052, Australia
SOURCE: J. Immunol. Methods (1992), 146(2), 213-18
CODEN: JIMMBG; ISSN: 0022-1759
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A rapid sandwich enzyme immunoassay format is described where conjugate is lyophilized within the well in which the test reaction will occur. The format is straight forward to manuf., has a prolonged shelf life, and eliminates one incubation and wash step from the usual test procedure. The technol. was applied to the development of a rapid assay for the identification of snake venom in clin. specimens. The resultant assay was specific and sensitive, provided rapid results, and was appropriate for field use.

L38 ANSWER 15 OF 15 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 91354147 MEDLINE

DOCUMENT NUMBER: 91354147 PubMed ID: 1883290
TITLE: Development and evaluation of a rapid absorbed enzyme immunoassay test for the diagnosis of Johne's disease in cattle.
AUTHOR: **Cox J C; Drane D P**; Jones S L; Ridge S; Milner A R
CORPORATE SOURCE: Commonwealth Serum Laboratories, Parkville, Victoria.
SOURCE: AUSTRALIAN VETERINARY JOURNAL, (1991 May) 68 (5) 157-60.
Journal code: 9IE; 0370616. ISSN: 0005-0423.
PUB. COUNTRY: Australia
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199109
ED Entered STN: 19911020
Last Updated on STN: 19911020
Entered Medline: 19910930

AB An absorbed enzyme immunoassay (EIA) test for Johne's disease in cattle was developed in which absorption of cross-reacting antibodies occurred as a rapid reaction in solution rather than overnight with whole organisms and a subsequent centrifugation step. Total test time was reduced to less than 2 h with a minimum of manipulations. The test was evaluated in cattle herds from Johne's disease-endemic and Johne's disease-free regions of Australia. Specificity was 99.8%. Calculations of sensitivity were affected by the history of the herd under test. However, the EIA detected in excess of 80% of animals before onset of clinical disease and 65% of faecal shedders were EIA positive on, or before, first detection of Mycobacterium paratuberculosis in their faeces. The test should aid epidemiological studies and be a useful tool in the management and control of Johne's disease.

FILE 'HOME' ENTERED AT 14:54:26 ON 24 APR 2001

** May contain prev. viewed citations

FILE 'CAPLUS' ENTERED AT 10:43:12 ON 25 APR 2001

L1 6908 SEA FILE=CAPLUS ABB=ON PLU=ON PHOSPHATIDYL GLYCEROL OR PHOSPHATIDYLGLYCEROL
L2 1736 SEA FILE=CAPLUS ABB=ON PLU=ON L1 AND (ANTIGEN OR PROTEIN)
L3 236 SEA FILE=CAPLUS ABB=ON PLU=ON L2 AND CHARG?
L4 57 SEA FILE=CAPLUS ABB=ON PLU=ON L3 AND POSITIV?
L5 39 SEA FILE=CAPLUS ABB=ON PLU=ON L4 AND NEGATIV?
L6 1 SEA FILE=CAPLUS ABB=ON PLU=ON L5 AND ((CYTOTOX? OR CYTO TOX?)(S)(T(W)(CELL OR LYMPHOCYT?)))

L1 6908 SEA FILE=CAPLUS ABB=ON PLU=ON PHOSPHATIDYL GLYCEROL OR PHOSPHATIDYLGLYCEROL
L2 1736 SEA FILE=CAPLUS ABB=ON PLU=ON L1 AND (ANTIGEN OR PROTEIN)
L3 236 SEA FILE=CAPLUS ABB=ON PLU=ON L2 AND CHARG?
L4 57 SEA FILE=CAPLUS ABB=ON PLU=ON L3 AND POSITIV?
L5 39 SEA FILE=CAPLUS ABB=ON PLU=ON L4 AND NEGATIV?
L7 3 SEA FILE=CAPLUS ABB=ON PLU=ON L5 AND (INFECTION OR HIV OR HTLV OR AIDS OR HUMAN(3W)VIRUS OR ACQUIRED(2W)SYNDROM? OR HEPATIT? OR TB OR TUBERCULOS? OR PARASIT?(3A)(CONDITION OR DISEAS? OR DISORDER) OR MELANOM? OR CANCER? OR CARCIN? OR NEOPLAS? OR TUMOUR OR TUMOR)

L8 3 L6 OR L7

L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:592580 CAPLUS
DOCUMENT NUMBER: 133:191986
TITLE: Immunogenic complexes and methods relating thereto
INVENTOR(S): Cox, John Cooper; Drane, Debbie Pauline
PATENT ASSIGNEE(S): CSL Limited, Australia
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000048630	A1	20000824	WO 2000-AU110	20000217

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,

VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 1999-8735 A 19990217
AU 1999-1861 A 19990727

AB The present invention relates generally to an immunogenic complex comprising a **charged** org. carrier and a **charged** **antigen** and, more particularly, a **neg.** **charged** org. carrier and a **pos.** **charged** **antigen**. The complexes of the present invention are useful, inter alia , as therapeutic and/or prophylactic agents for facilitating the induction of a **cytotoxic T-lymphocyte** response to an **antigen**.

IT **Hepatitis**
(B; immunogenic complexes **neg.** **charged** org. carrier and **pos.** **charged** **antigen** as vaccine for inducing **cytotoxic T** **lymphocyte** response)

IT **Proteins**, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C, Helicobacter pylori; immunogenic complexes **neg.** **charged** org. carrier and **pos.** **charged** **antigen** as vaccine for inducing **cytotoxic** **T lymphocyte** response)

IT **Hepatitis**
(C; immunogenic complexes **neg.** **charged** org. carrier and **pos.** **charged** **antigen** as vaccine for inducing **cytotoxic T** **lymphocyte** response)

IT **Proteins**, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E, Helicobacter pylori; immunogenic complexes **neg.** **charged** org. carrier and **pos.** **charged** **antigen** as vaccine for inducing **cytotoxic** **T lymphocyte** response)

IT **Proteins**, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E6; immunogenic complexes **neg.** **charged** org. carrier and **pos.** **charged** **antigen** as vaccine for inducing **cytotoxic T** **lymphocyte** response)

IT Transcription factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E7; immunogenic complexes **neg.** **charged** org. carrier and **pos.** **charged** **antigen** as vaccine for inducing **cytotoxic T** **lymphocyte** response)

IT **Antigens**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NY-ESO-1; immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT Immunostimulants
(adjuvants, ISCOMATRIX; immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT Immunostimulants
(adjuvants, ISCOMs, polytope; immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT Immunostimulants
(adjuvants; immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT Drug delivery systems
(carriers, **neg. charged**; immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT **T cell** (lymphocyte)
(**cytotoxic**; immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT Helicobacter pylori
Human immunodeficiency **virus**
Human papillomavirus
Melanoma
Neoplasm
Protein sequences
Tuberculosis
Vaccines
(immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT Cardiolipins
Glycerophospholipids
Lipid A
Phosphatidic acids

Phosphatidylglycerols
Phosphatidylinositols
Phospholipids, biological studies
Saponins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT Microorganism
Parasite
(**infection**; immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT **Infection**
(microbial; immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT Lipid A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monophosphates; immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT Carriers
(**neg. charged**; immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT Mammary gland
Prostate gland
(**neoplasm**; immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT **Antigens**
Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pos. charged**; immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT 124454-83-7 127902-44-7 132326-72-8 136671-81-3 202815-16-5 202815-17-6 288855-69-6 289054-26-8
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(immunogenic complexes **neg. charged** org. carrier and **pos. charg d antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT 4537-77-3, Dipalmitoylphosphatidyl glycerol 171092-39-0, OM 174
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunogenic complexes **neg. charged** org. carrier and **pos. charged antigen** as vaccine for inducing **cytotoxic T lymphocyte** response)

IT 289042-31-5
RL: PRP (Properties)
(unclaimed sequence; immunogenic complexes and methods relating thereto)

REFERENCE COUNT: 5
REFERENCE(S):
(1) Callahan, P; Pharmaceutical Research 1991, V8(7), P851 CAPLUS
(2) Friede, M; Molecular Immunology 1993, V30(6), P539 CAPLUS
(3) Morein; EP 0109942 A 1984 CAPLUS
(4) Morein; EP 0180564 A 1986 CAPLUS
(5) Nakanishi, T; Biochemical and Biophysical Research Communications 1997, V240(3), P793 CAPLUS

L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:466906 CAPLUS
DOCUMENT NUMBER: 129:199563
TITLE: Interaction of a basic amphipathic peptide from the carboxyterminal part of the **HIV** envelope **protein** gp41 with **negatively charged** lipid surfaces
AUTHOR(S): Trommeshauser, Dirk; Galla, Hans-Joachim
CORPORATE SOURCE: Institute of Biochemistry, Westfalische Wilhelms-Universitat Munster, Munster, D-48149, Germany
SOURCE: Chem. Phys. Lipids (1998), 94(1), 81-96
CODEN: CPLIA4; ISSN: 0009-3084
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The interaction of the **pos. charged** synthetic amphipathic peptide fragment gp41828 corresponding to a segment from the carboxyterminal region of the **HIV** envelope glycoprotein gp41 with lipid monolayers spread at the air-water interface has been studied by film balance measurements. The peptide itself does not form a stable monolayer but interacts with

phospholipids spread together on the aq. surface. Upon compression of a mixed phosphatidylcholine-peptide monolayer the peptide is irreversibly squeezed out of the lipid-peptide monolayer. In contrast, with **neg. charged** **phosphatidylglycerol** stable lipid-peptide monolayers are formed even in the presence of up to 30 mol% peptide. The monolayer may be expanded and compressed repeatedly without significant loss of substance. After addn. of calcium ions to the subphase of a **phosphatidylglycerol**-peptide monolayer the peptide is to some extent excluded from the monolayer. In contrast to phosphatidylcholine monolayers this process is partly reversible and the excluded material is reincorporated into the film during subsequent expansion. We conclude that attached to the headgroups of the lipid monolayer a peptide-layer stabilized at the surface by electrostatic interactions is formed. The surface action may lead to rigidified lipid-peptide domains causing an increased membrane permeability which might correspond to a cytopathol. function of the **protein** fragment.

IT Monolayers
(interaction of basic amphipathic peptide from carboxyterminal part of the **HIV** envelope **protein** gp41 with **neg. charged** lipid surfaces)

IT Lipids, biological studies
Lipopeptides
Phosphatidylglycerols
RL: BPR (Biological process); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(interaction of basic amphipathic peptide from carboxyterminal part of the **HIV** envelope **protein** gp41 with **neg. charged** lipid surfaces)

IT gp41 (env glycoprotein)
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(interaction of basic amphipathic peptide from carboxyterminal part of the **HIV** envelope **protein** gp41 with **neg. charged** lipid surfaces)

L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:738548 CAPLUS
DOCUMENT NUMBER: 128:72153
TITLE: Interactions of a tetravalent branched peptide from VP3 capsid **protein** of **hepatitis** A virus with monolayers as biomembrane models
AUTHOR(S): Alsina, Asuncion; Perez, Jose Antonio; Garcia, Monica; Reig, Francisca; Haro, Isabel
CORPORATE SOURCE: Physicochemical Unit, Faculty of Pharmacy, University of Barcelona, Barcelona, 08028, Spain

SOURCE: Supramol. Sci. (1997), 4(3-4), 195-199
CODEN: SUSCFX; ISSN: 0968-5677
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The interactions between a synthetic multiple antigenic peptide contg. four units of a peptide corresponding to the sequence (110-121) of VP3 **protein** of the **hepatitis** A virus, termed MAP4-VP3(110-121), and phospholipids as the main components of biol. membranes have been studied in detail. Surface activity of the multiple antigenic peptide was detd. as a function of its bulk concn. in an aq. soln. Satn. was reached at 0.33 .mu.M concn. The ability of the peptide to insert into lipid monolayers of dipalmitoyl phosphatidylcholine, dipalmitoyl **phosphatidylglycerol** and stearyl amine was detd. The peptide interacts preferably with the **pos**. phospholipid according to its **neg**. **charge**.

IT Capsid **proteins**
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(VP3; interactions of a tetravalent branched peptide from VP3 capsid **protein** of **hepatitis** A virus with monolayers as biomembrane models)

IT **Hepatitis** A virus
Monolayer (membrane)
(interactions of a tetravalent branched peptide from VP3 capsid **protein** of **hepatitis** A virus with monolayers as biomembrane models)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, CANCERLIT' ENTERED AT 10:47:48 ON 25 APR 2001)

L9 1 S L6
L10 15 S L7
L11 15 S L9 OR L10
L12 10 DUP REM L11 (5 DUPLICATES REMOVED)

L12 ANSWER 1 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-571930 [53] WPIDS
DOC. NO. CPI: C2000-170417
TITLE: Immunogenic complexes comprising **negatively charged** organic carrier adjuvants and **positively charged** **antigens** for use as vaccines against microbial **infection** and **cancer**.
DERWENT CLASS: B04 D16
INVENTOR(S): COX, J C; DRANE, D P
PATENT ASSIGNEE(S): (CSLC-N) CSL LTD
COUNTRY COUNT: 90

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000048630	A1	20000824	(200053)*	EN	111

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000026515 A 20000904 (200103)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000048630	A1	WO 2000-AU110	20000217
AU 2000026515	A	AU 2000-26515	20000217

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000026515	A	Based on	WO 200048630

PRIORITY APPLN. INFO: AU 1999-1861 19990727; AU 1999-8735 19990217

AN 2000-571930 [53] WPIDS

AB WO 200048630 A UPAB: 20001023

NOVELTY - An immunogenic complex comprising a **charged** organic carrier and a **charged antigen** which are electrostatically associated, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a vaccine composition comprising as the active component a complex as above, together with one or more carriers and/or diluents;

(2) eliciting, inducing or otherwise facilitating, in a mammal, an immune response to an **antigen**, comprising administering to the mammal an effective amount of the novel complex or the vaccine of (1); and

(3) an agent for inhibiting, halting, delaying or preventing the onset or progression of a disease or condition, comprising the novel complex or the vaccine of (1).

ACTIVITY - Virucide; Hepatropic; Antiinflammatory; **Tuberculostatic**; Cytostatic. No biological data is given.

MECHANISM OF ACTION - Immunogenic complex; Vaccine.

USE - The complex induces a **cytotoxic T lymphocyte** (CTL) response. The complex and/or vaccine can be used to treat a disease in a mammal, where the complex/vaccine elicits, induces or otherwise facilitates an immune response which inhibits, halts, delays or prevents the onset or progression of the disease condition. In particular, the disease is a condition resulting form a microbial **infection** or **cancer**. Microbial **infections** include **human** immunodeficiency **virus (HIV)**, **hepatitis** B, **hepatitis** C, **tuberculosis** or a **parasitic condition** and the **cancer** is **melanoma**, prostate **cancer** or breast **cancer** . All claimed.

ADVANTAGE - The complexes and vaccines co-deliver **antigen** and adjuvant at the same time to the same **antigen** presenting cell, which is often essential for induction of appropriate immune responses.

Dwg.0/15

L12 ANSWER 2 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-350562 [30] WPIDS
DOC. NO. CPI: C2000-106601
TITLE: New combinations of substances, useful for the preparation of drug carriers, drug depots, in bioengineering, for genetic manipulations or diagnostic applications.
DERWENT CLASS: A25 A96 B04 D16
INVENTOR(S): CEVC, G
PATENT ASSIGNEE(S): (IDEA-N) IDEA INNOVATIVE DERMALE APPLIKATIONEN GM
COUNTRY COUNT: 79
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000024377	A1	20000504	(200030)*	EN	87
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN					
AU 9914350	A	20000515	(200039)		
EP 1039880	A1	20001004	(200050)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
NO 2000003287	A	20000823	(200054)		
BR 9814415	A	20001010	(200055)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000024377	A1	WO 1998-EP6750	19981023
AU 9914350	A	WO 1998-EP6750	19981023
		AU 1999-14350	19981023
EP 1039880	A1	EP 1998-958234	19981023
		WO 1998-EP6750	19981023
NO 2000003287	A	WO 1998-EP6750	19981023
		NO 2000-3287	20000622
BR 9814415	A	BR 1998-14415	19981023
		WO 1998-EP6750	19981023

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9914350	A	Based on	WO 200024377
EP 1039880	A1	Based on	WO 200024377
BR 9814415	A	Based on	WO 200024377

PRIORITY APPLN. INFO: WO 1998-EP6750 19981023

AN 2000-350562 [30] WPIDS

AB WO 200024377 A UPAB: 20000624

NOVELTY - New combinations of substances comprise 2 amphipatic substances in a liquid medium which can be combined with a medicinal or biological substance

DETAILED DESCRIPTION - A novel combination of substances is claimed, at least 2 of which exhibit amphipatic properties when contacted with a suitable liquid medium, the 2 substances differing in their solubility in this medium and the combination being capable of forming extended surfaces, especially membrane surfaces in contact with the medium, such that molecules of an amphipatic third substance can associate with the surface, where the at least 2 substances are selected so that:

(a) the substance which is more soluble in the liquid medium than the other substance forms less extended surfaces than the other substance of the combination; and

(b) molecules of the third substance are more likely to associate with the extended surfaces formed by the other at least 2 substances combined than with an extended surface formed by the other, less soluble substance alone.

INDEPENDENT CLAIMS are also included for:

(1) a combination of substances, at least 2 of which exhibit amphipatic properties when contacted with a suitable medium, the 2 substances being capable of forming, at least when combined, an extended surface, especially a membrane surface, in contact with the medium, the surface carrying a net electric **charge**, such

that molecules of a further amphipatic substance with a net electric **charge** can associated with the surface, and the net **charge** density of the surface and the net **charge** of the amphipatic molecules associating with the surface have the same sign (both **negative** or both **positive**);

(2) a combination of substances, at least 2 of which exhibit amphipatic properties when contacted with a suitable liquid medium, the 2 substances differing in their solubility in this medium and being capable of forming, at least when combined, extended surfaces, especially membrane surfaces, in contact with the medium, such that molecules of an amphipatic third substance can associated with the surfaces, the at least 2 substances being selected so that:

(a) the substance which is more soluble in the liquid medium than the other substance forms less extended surfaces than the other substance of the combination;

(b) molecules of the third substance are more likely to associate with the extended surfaces formed by the combination of the 2 substances than with an extended surface formed only by the other, less soluble substance; and

(c) the surfaces formed by the combined substances as well as the molecules of the third substance likely to associate with the surface, are both **negatively charged** or both **positively charged**;

(3) a method of preparing a formulation of an active agent, especially a biologically, cosmetically and/or pharmaceutically active agent, characterized by selecting at least 2 amphipatic substances, which differ in their solubility in a suitable liquid medium, such substances being capable of forming an extended surface, especially a membrane surface, at least when combined in contact with the medium; such that an extended surface formed by the combination of substances is capable of attracting and associating with the active agent to a greater extent than the surface formed only from the substance which is less soluble in the liquid medium and forms more extended surfaces than the other substances alone;

(4) a method for the preparation of a formulation for non-invasive application of various agents, such as anti-diabetic agents, growth factors, immunomodulators, enzymes, recognition molecules, etc, or adrenosorticostatica, adrenolitica, etc, where surfaces capable of associating with the agent molecules are formed from at least one amphipatic substance, at least one hydrophilic fluid, at least one edge active substance or surfactant, at least one agent, and, other customary ingredients, which together form the formulation.

USE - The combinations can be used for the preparation of drug carriers, drug depots, in bioengineering, in genetic manipulations, in separation technology, for (bio)processing, for diagnostic applications, for stabilizing surface associated molecules such as (derivatized) **proteins**, polypeptides, polynucleotides, or

polysaccharides and/or in catalyzing processes which involve such molecules in the surface-associated state (claimed). They can also be used to affect the kinetics and/or the reversibility of association or dissociation between the surface-associating molecules and a complex, adaptable surface, whereby the higher surface **charge** density and/or greater surface softness and/or surface defect density speeds up the association, or the corresponding reduction slows down the rate of association or else induces partial molecular dissociation (claimed).
Dwg.0/12

L12 ANSWER 3 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-205859 [18] WPIDS
DOC. NO. CPI: C2000-063576
TITLE: Epipodophyllotoxin liposomal formulation, uses phospholipid and/or sterol solubilizers, does not cause fluid overload, has increased efficiency in **cancer** and proliferative disorders and reduced general toxicity.
DERWENT CLASS: A96 B04 B05
INVENTOR(S): GUPTA, S K; SENGUPTA, S; VELPANDIAN, T
PATENT ASSIGNEE(S): (ALLI-N) ALL INDIA INST MEDICAL SCI
COUNTRY COUNT: 77
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000009071	A2	20000224	(200018)*	EN	54
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 2000016789	A	20000306	(200030)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000009071	A2	WO 1999-IN37	19990810
AU 2000016789	A	AU 2000-16789	19990810

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000016789	A Based on	WO 200009071

PRIORITY APPLN. INFO: IN 1998-2337 19980811

Searcher : Shears 308-4994

AN 2000-205859 [18] WPIDS
AB WO 200009071 A UPAB: 20000412
NOVELTY - Novel liposomal formulation useful in treatment of **cancer** and other proliferative diseases, containing a mixture of at least 0.1-50 mol% of epipodophyllotoxin or its analogs or derivatives, phospholipids and/or sterols, both in molar ratio of 1-15.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for processes for their preparation; and a kit containing (I) with cryoprotectants and antioxidants.

ACTIVITY - Anticancer; antiproliferative.

MECHANISM OF ACTION - **Tumor** cells require much nutrient, and attract the liposome formulation. Due to the improved formulation, higher doses of almost insoluble epipodophyllotoxin are introduced into the cells with less dilution. Epipodophyllotoxins inhibit DNA topoisomerase II activity, and block transcription to RNA restricting formation of **proteins** and cell division in **tumor** cells.

USE - The formulation is used in the treatment of **cancer** and other proliferative diseases, e.g., psoriasis; particularly small cell lung **cancer**. For convenience, a kit of the formulation is recommended, but antioxidants and cryoprotectants are advisable for storage in this form.

ADVANTAGE - Prior art formulations have required excessive dilution to solubilize the epipodophyllotoxin, with possibility of variable dosage, heart failure, hypertension, hypersensitivity, and body weight loss, as serious side effects. The present formulation is stable, has a lower toxicity profile, a reduced clearance rate, and an increase in AUC over free drug.

Dwg.0/0

L12 ANSWER 4 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-136656 [12] WPIDS
CROSS REFERENCE: 1998-387767 [33]
DOC. NO. NON-CPI: N2000-102226
DOC. NO. CPI: C2000-041816
TITLE: Mucosal administration of substance e.g. vaccine by contacting mucosal surface with substance in combination with optionally coated natural polymer core e.g. crosslinked polysaccharide .
DERWENT CLASS: B07 P34
INVENTOR(S): BETBEDER, D; DE MIGUEL, I; ETIENNE, A; KRAVTZOFF, R; MAJOR, M
PATENT ASSIGNEE(S): (BIOV-N) BIOVECTOR THERAPEUTICS SA
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

US 6017513	A	20000125 (200012)*	27

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6017513	A	CIP of	US 1996-774920	19961227
			US 1997-987436	19971209

PRIORITY APPLN. INFO: US 1997-987436 19971209; US 1996-774920 19961227

AN 2000-136656 [12] WPIDS

CR 1998-387767 [33]

AB US 6017513 A UPAB: 20000308

NOVELTY - Mucosal administration of substances to mammals comprises contacting a mucosal surface with the substance in combination with Biovector core comprising natural polymer and/or its hydrolysate that is uncoated or partially or completely coated with no more than one layer comprising lipid compound covalently bonded to the core or an amphiphilic compound.

ACTIVITY - Drug delivery.

The delivery system is used for mucosal administration of substances to mammals (claimed) including therapeutic or prophylactic agents (radiopharmaceutical, analgesic, anesthetic, anorectic, anti-anemic, anti-asthmatic, anti-diabetic, antihistamine, anti-inflammatory, antibiotics, antimuscarinic, antineoplastic, antiviral, cardiovascular drug, CNS depressant, CNS stimulator, antidepressant, anti-epileptic, anxiolytic, hypnotic, sedative, anti-psychotic, beta blocker, hemostatic, hormone, vasodilator, vasoconstrictor, vitamin, vaccines against pathogens including bacteria, viruses, yeasts or fungi, specifically influenza virus (preferred), cytomegalovirus, **human** immunodeficiency **virus**, papilloma **virus**, respiratory syncytial virus, poliomyelitis virus, pox virus, measles virus, arbor virus, Coxsackie virus, herpes virus, hantavirus, **hepatitis** virus, Lyme disease virus, mumps virus or rotavirus, Neisseria, Aerobacter, Pseudomonas, Porphyromonas, Salmonella, Escherichia, Pasteurella, Shigella, Bacillus, Helibacter (sic), Corynebacterium, Clostridium, Mycobacterium, Yersinia, Staphylococcus, Bordetella, Brucella, Vibrio or Streptococcus, Plasmodium, Schisostoma or Candida, diagnostic agents such as contrast or imaging agent e.g. that detect corneal irregularities or those labeled with detectable groups (radioactive, magnetic or fluorescent), small chemical molecules (organic, inorganic or organo-metallic molecules) or biological molecules (amino acid, oligopeptide, peptide, **protein**, glycoprotein, lipoprotein, proteoglycan,

lipopolysaccharide, fatty acid, eicosanoid, lipid, triglyceride, phospholipid, glycolipid, nucleoside, nucleotide, nucleic acid, DNA molecule, RNA molecule, monosaccharide, oligosaccharide or polysaccharide) (claimed) as well as cytokines, growth factors, enzymes, **antigens** (including epitopes of **antigens** and haptens), antibodies, hormones, (natural and synthetic hormones and their derivatives), co-factors, receptors, enkephalins, endorphins, neurotransmitter s and nutrients such as insulin, interferon (alpha -, beta - or gamma -IFN), interleukins (IL-1 to IL-15), interleukin receptors (IL-1 receptor), calcitonin, erythropoeitin, thrombopoietin, epidermal growth factor and insulin-like growth factor-1. It can also be used to detect irregularities within the respiratory tract, digestive tract, auditory canal, urethra, rectum or any part of mammal with mucosal membrane and to deliver contrast agents for magnetic resonance imaging.

Influenza hemagglutinin (HA) was delivered by Biovectors to female mice, with 5 mu g HA applied intranasally in 20 or 50 mu l of phosphate-buffered saline solution or suspension, either alone or in Biovector formulation. One group of animals was subjected to light ether anesthesia, while the others were awake. Administration of 20 mu l on the outer nostrils of awake animals restricted the **antigen** to the upper respiratory tract. Volume of 50 mu l directly into the nostrils of anesthetized animals resulted in deposition of at least some **antigen** in the lower respiratory tract and lung as well as in the nasal cavity. Four different Biovectors were used: (Q) **positive** and (P) **negatively charged** light Biovectors either re-suspended - (1Q) and (1P) - or dispersed (2Q) and (2P). Influenza virus subunit **antigen** was either pre-loaded in the Biovectors or post-loaded (admixed immediately prior to administration). **Antigen** alone was used as control (3). Mice were sacrificed at day 28 and serum samples from the vena porta analyzed by direct enzyme-linked immunosorbent assay (ELISA). Serum immunoglobulin G titers (geometric mean) determined as reciprocal of sample dilution corresponding to absorbance at 492 nm of 0.2 above background were as follows in unanesthetized animals: (1Q) pre-loaded = 10, post-loaded = 20; (1P) pre-loaded = 400, post-loaded = 30; (2Q) pre- and post-loaded = 2,000; (2P) pre- and post-loaded = 200, and as follows in anesthetized animals: (1Q) = 30; (1P) = 30; (2Q) 4,000; (2P) = 60. Control was 100 for unanesthetized animals and 200 in anesthetized animals.

MECHANISM OF ACTION - None given.

ADVANTAGE - The system is capable of delivering substances to animals (including humans) efficiently and avoiding disadvantages of the prior art. The carrier directs substances to the mucosa in a non-specific manner, is capable of being loaded with the substance immediately prior to administration, is of a size susceptible to

microfiltration for sterilization avoiding need for preservatives and it is stable for up to 12 months, even one or more years. Biovectors have larger relative surfaces and volumes than larger microspheres or nanospheres and multiple substances can be delivered per Biovector.
Dwg.0/11

L12 ANSWER 5 OF 10 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:489356 BIOSIS
DOCUMENT NUMBER: PREV200000489477
TITLE: The effect of lipid composition and physical state of phospholipid monolayer on the binding and incorporation of a basic amphipathic peptide from the C-terminal region of the **HIV** envelope **protein** gp41.
AUTHOR(S): Trommeshauser, Dirk; Krol, Silke; Bergelson, Lev D.; Galla, Hans-Joachim (1)
CORPORATE SOURCE: (1) Institute of Biochemistry, Westfaelische Wilhelms-Universitaet Muenster, Wilhelm-Kiemm-Strasse 2, 48149, Muenster Germany
SOURCE: Chemistry and Physics of Lipids, (September, 2000) Vol. 107, No. 1, pp. 83-92. print.
ISSN: 0009-3084.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The interaction of a peptide identical to the carboxy terminal region of the envelope glycoprotein gp41828 of **HIV** with **negatively charged** phospholipids in a monolayer was studied by a Wilhelmy film balance. No significant interaction of the peptide with a monolayer composed of pure neutral but a strong affinity to **negatively charged** phospholipids could be observed. In mixed phospholipid monolayers the binding of the gp41828 is primarily limited by the amount of acidic phospholipids. The physical state of the monolayer is another important parameter for binding. Clustering of **negatively charged** phospholipids and the surface pressure are crucial. Ca2+ ions strongly interfere with the peptide-lipid interaction up to complete abolishment. The effects observed are dependent on the nature of the acidic lipid. **Phosphatidylglycerol** was found to be more sensitive than phosphatidylserine. The significance of the results for processes like virus assembly and budding will be discussed.

L12 ANSWER 6 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-620582 [53] WPIDS
DOC. NO. CPI: C1999-181230
TITLE: Novel contrast agent for ultrasound imaging of

subject, particularly myocardium and other tissues.

DERWENT CLASS: B05

INVENTOR(S): CUTHBERTSON, A; ERIKSEN, M; FRIGSTAD, S; OSTENSEN, J; RONGVED, P; SKURTVEIT, R; TOLLESHAUG, H

PATENT ASSIGNEE(S): (ERIK-I) ERIKSEN M; (NYCO-N) NYCOMED IMAGING AS; (MARS-I) MARSDEN J C

COUNTRY COUNT: 87

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9953963	A1	19991028	(199953)*	EN	80
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9936172	A	19991108	(200014)		
BR 9909822	A	20001219	(200103)		
NO 2000005250	A	20001218	(200106)		
EP 1073473	A1	20010207	(200109)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9953963	A1	WO 1999-GB1221	19990422
AU 9936172	A	AU 1999-36172	19990422
BR 9909822	A	BR 1999-9822	19990422
		WO 1999-GB1221	19990422
NO 2000005250	A	WO 1999-GB1221	19990422
		NO 2000-5250	20001019
EP 1073473	A1	EP 1999-918133	19990422
		WO 1999-GB1221	19990422

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9936172	A	Based on	WO 9953963
BR 9909822	A	Based on	WO 9953963
EP 1073473	A1	Based on	WO 9953963

PRIORITY APPLN. INFO: GB 1998-8599 19980422

AN 1999-620582 [53] WPIDS

AB WO 9953963 A UPAB: 19991215

NOVELTY - The contrast agent is formulated by dispersing gas component as a stabilized injectable gas dispersion and the diffusible component as an injectable stabilized oil-in-water emulsion, such that the material present at the surface of the dispersed gas has affinity for the material present at the surface of the dispersed diffusible component.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the method of generating enhanced images of human or non-human animal subject which comprises injecting the aqueous medium into the vascular system of the subject, followed by injecting the oil-in-water emulsion.The emulsion is injected before, during or after injection of the aqueous medium to generate an ultrasound image of at least a portion of the subject.

USE - The contrasting agent is used for ultrasonic visualization of a subject, particularly myocardium and other tissues. Also for imaging other capillary systems such as kidney, liver, spleen, thyroid, skeletal muscle, breast and prostate. The contrast agent may also be used as delivery agents or as vehicles of therapeutically active substances. The contrasting agent may be used therapeutically by intervenous injection of a high dose for treating **tumor**, by exposing the **tumor** to local ultrasound irradiation, particularly to treat liver, breast, thyroid and prostate **tumours**.

ADVANTAGE - The contrast agent may readily permit effective imaging of tissue such as the myocardium using conventional B- mode scanning techniques. The droplet size of emulsion intended for intravenous injection should be less than 10 mu m, desirably less than 0.1-7 mu m in order to facilitate unimpeded passage through the pulmonary system. If desired, the diffusible component may also be formulated as a micro-emulsions which have good thermodynamic stability. Substantially, lower doses of diffusible component (20 nl diffusible component/kg body weight) containing emulsion can also be used to obtain images comparable to those observed in WO-A-9817324. The diffusible component in the emulsion has the capability of at least 100-fold increase in volume when evaporated, thereby preventing the rise in risk of embolism. The temperature of the dispersed gas and/or emulsion, prior to administration can be manipulated by the use of constituents which react exothermically under the influence of ultrasound radiation, to ensure maximum volatilization of the diffusible component and to enhance growth of the dispersed gas. The exposed gas surface, due to absence of encapsulating material, may cause the contrast agent to exhibit exceptionally favorable acoustic properties due to high backscatter and low energy absorption. The control of the duration of retention of the dispersed gas may be achieved by appropriate adjustment of the dose and/or formulation of the diffusible component, particularly the nature and degree of affinity between the gas component and diffusible component. The effective rate of transport

of the diffusible component may be controlled, by adjusting the viscosity of the dispersed gas phase composition and/or the diffusible component composition, by incorporating one or more bio-compatible viscosity enhancers such as X-ray contrast agents, polyethylene glycols, carbohydrate, **proteins**, polymers or alcohols in the formulation. Reduction in the droplets size of the diffusible component will lead to an increase in the overall number of droplets, and so may enhance the rate of transfer by reducing the mean interparticle distance between the gas microbubbles and emulsion droplets, and thus increasing the probability of collision and/or coalescence. Contrast agents containing bio-compatible azeotropic mixtures have effective echogenic lifetime in-vivo, as water solubility, fat solubility, diffusibility and pressure resistivity of the compounds such as fluorocarbons decrease with increasing molecular weight.
Dwg.0/0

L12 ANSWER 7 OF 10 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1998388603 MEDLINE
DOCUMENT NUMBER: 98388603 PubMed ID: 9721631
TITLE: Interaction of a basic amphipathic peptide from the carboxyterminal part of the **HIV** envelope **protein** gp41 with **negatively charged** lipid surfaces.
AUTHOR: Trommeshauser D; Galla H J
CORPORATE SOURCE: Institute of Biochemistry, Westfalische Wilhelms-Universitat Munster, Germany.
SOURCE: CHEMISTRY AND PHYSICS OF LIPIDS, (1998 Jul) 94 (1) 81-96.
Journal code: CZW; 0067206. ISSN: 0009-3084.
PUB. COUNTRY: Ireland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ED Entered STN: 19981006
Last Updated on STN: 19981006
Entered Medline: 19980921

AB The interaction of the **positively charged** synthetic amphipathic peptide fragment gp41(828) corresponding to a segment from the carboxyterminal region of the **HIV** envelope glycoprotein gp41 with lipid monolayers spread at the air-water interface has been studied by film balance measurements. The peptide itself does not form a stable monolayer but interacts with phospholipids spread together on the aqueous surface. Upon compression of a mixed phosphatidylcholine-peptide monolayer the peptide is irreversibly squeezed out of the lipid-peptide monolayer. In contrast, with **negatively charged**

ph sphatidylglycerol stable lipid-peptide monolayers are formed even in the presence of up to 30 mol% peptide. The monolayer may be expanded and compressed repeatedly without significant loss of substance. After addition of calcium ions to the subphase of a **phosphatidylglycerol**-peptide monolayer the peptide is to some extent excluded from the monolayer. In contrast to phosphatidylcholine monolayers this process is partly reversible and the excluded material is reincorporated into the film during subsequent expansion. We conclude that attached to the headgroups of the lipid monolayer a peptide-layer stabilized at the surface by electrostatic interactions is formed. The surface action may lead to rigidified lipid-peptide domains causing an increased membrane permeability which might correspond to a cytopathologic function of the **protein** fragment.

L12 ANSWER 8 OF 10 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1998:50565 SCISEARCH
THE GENUINE ARTICLE: YP313
TITLE: Interactions of a tetravalent branched peptide from VP3 capsid **protein** of **hepatitis** A virus with monolayers as biomembrane models
AUTHOR: Alsina A (Reprint); Perez J A; Garcia M; Reig F; Haro I
CORPORATE SOURCE: UNIV BARCELONA, FAC PHARM, PHYSICOCHEM UNIT, E-08028 BARCELONA, SPAIN (Reprint); CSIC, CID, DEPT PEPTIDE & PROT CHEM, ES-08034 BARCELONA, SPAIN
COUNTRY OF AUTHOR: SPAIN
SOURCE: SUPRAMOLECULAR SCIENCE, (SEP-DEC 1997) Vol. 4, No. 3-4, pp. 195-199.
Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, OXON, ENGLAND OX5 1GB.
ISSN: 0968-5677.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 12

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The interactions between a synthetic multiple antigenic peptide containing four units of a peptide corresponding to the sequence (110-121) of VP3 **protein** of the **hepatitis** A virus, termed MAP(4)-VP3(110-121), and phospholipids as the main components of biological membranes have been studied in detail. Surface activity of the multiple antigenic peptide was determined as a function of its bulk concentration in an aqueous solution. Saturation was reached at 0.33 mu M concentration. The ability of the peptide to insert into lipid monolayers of dipalmitoyl phosphatidylcholine, dipalmitoyl **phosphatidylglycerol** and stearyl amine was determined. The peptide interacts preferably with the **positive** phospholipid according to its

negative charge. (C) 1997 Elsevier Science Ltd.
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L12 ANSWER 9 OF 10 MEDLINE
ACCESSION NUMBER: 95284893 MEDLINE
DOCUMENT NUMBER: 95284893 PubMed ID: 7767388
TITLE: Role of interactions at the lipid-water interface for domain formation.
AUTHOR: Gawrisch K; Barry J A; Holte L L; Sinnwell T; Bergelson L D; Ferretti J A
CORPORATE SOURCE: Laboratory of Membrane Biochemistry and Biophysics, NIAAA, NIH, Rockville, MD 20852, USA.
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AB The lipid-water interface is critical for the packing of lipid molecules in membranes. We have demonstrated that lateral phase separation in membranes can be driven by electrostatic interactions such as those involving **charged** lipid species and oppositely **charged** peptides, in addition to hydration effects at the lipid-water interface. By using nuclear magnetic resonance (NMR), circular dichroism and fluorescence spectroscopy we have shown that binding of a 21-amino acid peptide containing six **positively charged** arginine residues to mixed phosphatidylcholine (PC)/**phosphatidylglycerol** (PG) membranes results in a conformational change in the peptide from a random coil to a helical structure and causes the formation of domains of **negatively charged** PG. Binding of the peptide to PG membranes disorders the lipid hydrocarbon chains. The strength of lipid-peptide binding at the interface, the conformational change in the peptide, and domain formation with the **negatively charged** lipid are coupled energetically. The lipid-peptide association constant is lower for membranes containing 20 mol% PG in PC/PG mixtures than for 100% PG membranes. We suggest that one of the factors that lower the association constant in PC/PG membranes is entropic energy of formation of PG domains. Besides electrostatic interactions, hydration of lipids is important for domain formation. We have shown that dipalmitoylphosphatidylcholine and dipalmitoylphosphatidylethanolamine separate under conditions of

decreased water activity. Furthermore, water activity controls lipid packing stress in the hydrocarbon core and the headgroups of membranes as demonstrated by induction of an inverse-hexagonal-to-lamellar phase transition in dioleoylphosphatidylethanolamine. (ABSTR ACT TRUNCATED AT 250 WORDS)

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AUTHOR: Gawrisch K; Han K H; Yang J S; Bergelson L D; Ferretti J A
CORPORATE SOURCE: Laboratory of Biophysical Chemistry, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland 20892.
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AB The interaction of the peptide fragment 828-848, called P828, from the carboxy-terminal region of the envelope glycoprotein gp41 of **HIV**-I with model membranes composed of phosphatidylcholine (PC) and **phosphatidylglycerol** (PG) was investigated using microelectrophoretic mobility of liposomes, fluorescence polarization of labeled lipids, NMR, and differential scanning calorimetry. The peptide binds to **negatively charged** lipid surfaces. No interaction between P828 and neutral PC surfaces is observed. The interaction between the peptide and the lipid is exclusively electrostatic with the six **positively charged** arginines of P828 acting as binding sites for PG. Circular dichroism measurements of P828 indicate that the peptide undergoes a transition from a random coil to an ordered conformation upon binding to **negatively charged** PG bilayers or SDS micelles, but not in the presence of neutral PC bilayers. The ordered structure has an apparent helical content of 60%. IN DOPG/DOPC mixtures containing 20 mol % DOPG, the peptide causes the formation of lipid domains enriched in DOPG, as assessed by measurement of fluorescence energy transfer between labeled PG and PC. The formation of these domains requires

energy and therefore reduces the strength of peptide binding to the lipid matrix. Our data support and quantitate the results from antibody binding studies [Haffar, O.K., Dowbenko, D. J., & Berman, P. W. (1988) J. Cell Biol. 107, 1677-1687] that the carboxy-terminal segment of the envelope glycoprotein gp41 interacts with microsomal membranes.

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